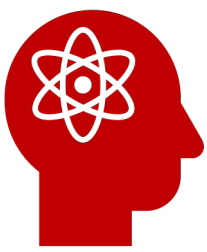
RUTGERS

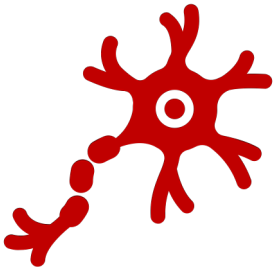
THE STATE UNIVERSITY
OF NEW JERSEY

Summer Undergraduate Research Fellow (SURF)

Final Presentations

July 28, 2022





Week	SURF Weekly Activities
1	Orientation and Tie Dye Lab Coats
	LinkedIn and Social Media Professional Engagement
2	Translational Research: Bridging Science from the Bench to the Bedside
3	Dr. John McGann (Rutgers) “The Changing Olfactory System in Health and Disease: Learning, Vaping, and (Sort of) Rehabilitation” and Dr. Emily Barrett (Rutgers) “Environmental Epidemiology: Prenatal Exposures and Child Health”
	Careers in Pharmaceutical Industry
4	Research Blitz: Science from Trainees
5	Science Communication: Distilling Your Message
	Environmental Sampling with Groundwork Elizabeth Trip
6	Careers, Networking, and Painting: Meet Alumni and Trainees
	Disseminating Science Through Effective Written and Graphical Abstracts
7	Mr. Paul Levesque (Bristol-Myers Squibb) Discovery Toxicology: Innovative Testing Models
8	Bristol-Myers Squibb Field Trip
	Developing Therapeutics to Counteract Chemical Weapon Toxicities - Drs. Joshua Gray (US Coast Guard) and Dr. Debra Laskin (Rutgers) & Group Photo
9	What Did We Learn from Environmental Field Sampling? Dr. Cathleen Doherty (Rutgers) & Abstract Peer Review
10	Research Symposium

Session I Presentations (11:00 a.m. – 12:00 p.m.)	
Presenter	**Mentor**
Karim Abdelhalim	Hu
Alden Ordaniel	Minko
Kyo Chang Lee	Suh
Chacko Jacob	Zheng
Mohamad Nasar Eddin	Chen
Faranguisse Sadrieh	DeLoid/Demokritou
Joshua Baw	Yang/Demokritou
Daniela Bermeo Grajales	Doherty/Buckley

Session II Presentations (12:15 p.m. – 1:15 p.m.)	
Presenter	**Mentor**
Betia Zeng	Laumbach
Justin Lee	An
Shine Wang	Aleksunes
Faythe Cooper	Aleksunes
Ruth Meletz	Aleksunes
Zachary Kobs	Roepke
Nivedita Krishnakumar	James
Daniel Luo	Zhou

Session III Presentations (1:30 p.m. – 2:30 p.m.)	
Presenter	**Mentor**
Rachel Sun	Laskin
Olympia Su	Joseph/Laskin
Benjamin Gelfand-Titiyevskiy	Smith/Laskin
Melissa Kudlak	Bellomo/Laskin
Sung Lee	Gow
Perel Rose	Gow
Sophie Gao	Guo
Mohammed Khedr	Kong


Biological
& Chemical

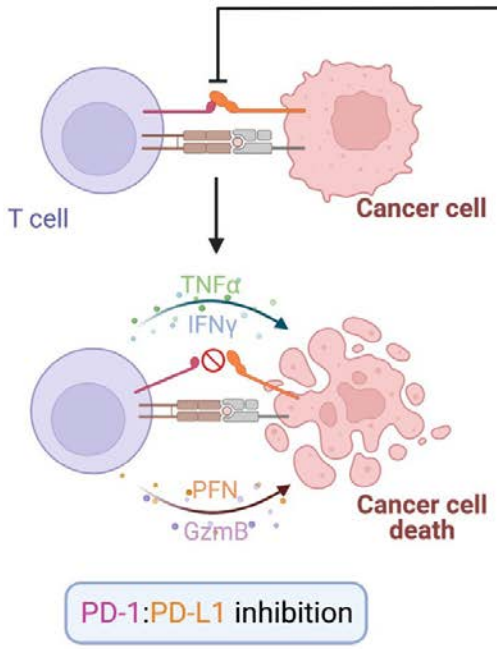

committed

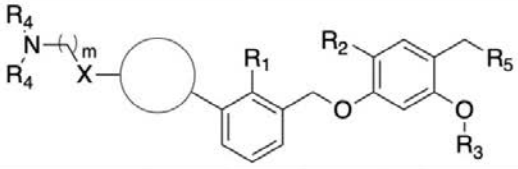

Wallows

Synthesis and Evaluation of Small Molecule Inhibitors of the PD-1/PD-L1 Protein-Protein Interaction

Karim Abdelhalim, Jeffrey Yang, Subhadwip Basu, Longqin Hu
Rutgers, The State University of New Jersey

Programmed cell death-1 receptor (PD-1) and programmed cell death-ligand 1 (PD-L1) are extracellular proteins located on T cells and antigen presenting cells, respectively. PD-1/PD-L1 protein-protein interaction (PPI) is normally involved in limiting the generation of autoreactive T cells. However, cancer cells highly express PD-L1 on their surface to escape immune detection. PD-1/PD-L1 PPI inhibitors can prevent cancer cells from evading the immune system. Monoclonal antibodies are the current standard therapy, but have limitations including higher costs and no oral bioavailability, which could be overcome by using small molecule inhibitors. This study aims to synthesize and evaluate three small molecules as inhibitors of the PD-1/PD-L1 PPI to explore the structure-activity relationships of the chemotype. The three target compounds were synthesized in 13 steps with overall yields between 1-6% and characterized by ^{1}H and ^{13}C-NMR spectroscopy and HRMS. Inhibitory activity of the target compounds with reference (LH1461) and control compounds were measured in a homogenous time-resolved fluorescence resonance energy transfer assay. The three synthesized analogs were found to be more potent than the reference compound LH1461 (2,986±43 nM). LH1469 with the ethylene linker and LH1470 with the propylene linker showed an IC_{50} of 574±103 nM and 507±123 nM, respectively. Most notably, LH1468 with the propionyl linker exhibited the best inhibitory activity in this series with an IC_{50} of 89±17 nM. LH1468, with its propionyl linker, could be considered as a potential lead for further optimization. Supported by Rutgers University Foundation, NIH R25ES020721 and the SURF program.





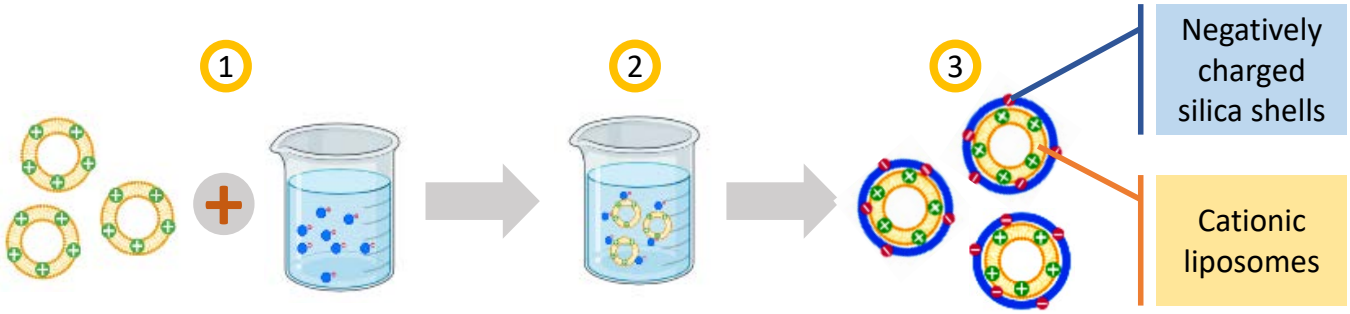
Compound ID	R_3	R_5	X	m	IC_{50} (nM)
LH1461	R_3-B	R_5-B	CO	1	2,986±43
LH1468	R_3-B	R_5-B	CO	2	89±17
LH1469	R_3-B	R_5-B	CH_2	1	574±103
LH1470	R_3-B	R_5-B	CH_2	2	507±123

Proposed Small Molecule Inhibitor Analogs

Liposomes with Silica Coated Shell for Protective Targeted Delivery of mRNA Vaccines

Alden Ordaniel, Andrew M. Shen, David Lee, Tamara Minko
Rutgers, The State University of New Jersey

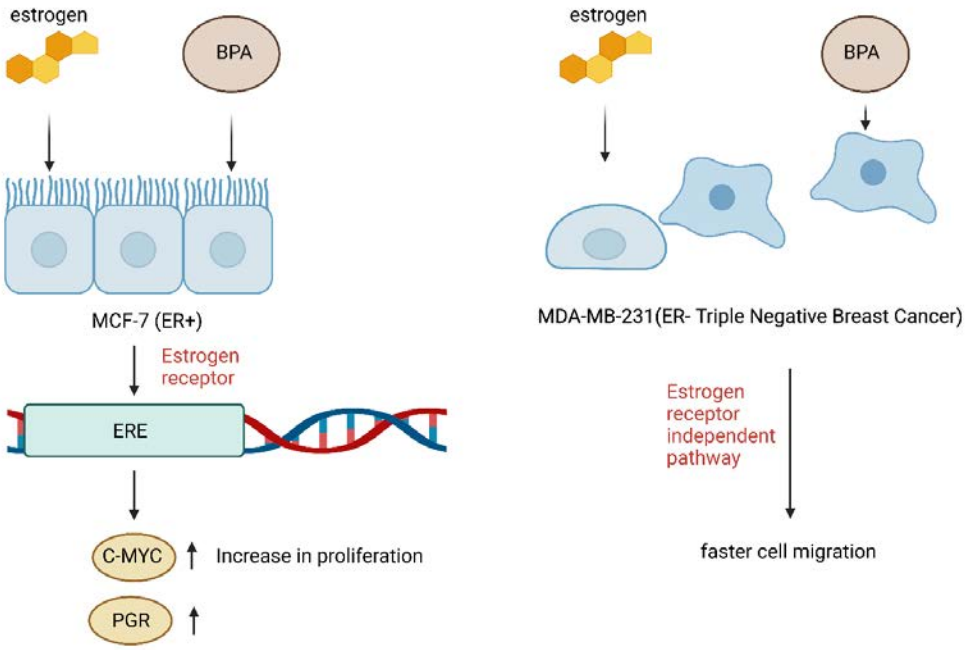
Liposomes and other nanosized lipid-based vesicles, are currently widely used in various drug/nucleic acid delivery applications. Development of vaccines, including cancer and COVID-19 vaccines, based on the use of nucleic acids delivered by lipid nanoparticles currently attracts the most attention of researchers. However, a wide clinical application of mRNA-based vaccines is substantially tampered by a low resistance of mRNA against destroying action of relatively high temperature during their storage and harsh conditions during their traffic after injections in the enzyme rich blood and body fluids towards the site of the most efficient vaccine application. The current project explores a possibility of substantial increasing in stability and resistance of mRNA encapsulated in silica coated lipid-based nanoparticles during the storage and nanoparticle journey inside the body after injection towards the antigen presenting cells. We hypothesize that the coating of cationic liposomes with protective silica shells can be augment the stability of the internalized drug. Such research can be translated to work into mRNA carrying lipid nanoparticles. Experiments on this stage of investigation were aimed at developing a method of rapid fabrication and characterization of such nanoparticles. We are currently developing an innovative method of coating of cationic (positively charged) lipid vehicles with anionic (negatively charged) silica shells. The general idea behind the method can be illustrated in three main steps (Figure 1). Cationic liposomes were mixed with a concentrated silica precursor solution (1) forming a stable colloid solution. The negatively charged silica nanoparticles are attracted to the positively charged lipid bilayer (2) finally resulting under carefully selected conditions in the formation of stable silica coated lipid nanoparticles (3). The source components and final nanoparticles were characterized by their zeta-potential and size using a dynamic light scattering (DLS) instrument. Stability of the final nanoparticles will be evaluated by assessing the degradation profile versus various concentrations of Triton-X 100, a surfactant. Preliminary experiments showed that upon addition of liposomes to the silica sol excess silica precipitate was generated by the end of the reaction. Upon characterizing the size, shows that a heterogenous distribution with large particles (> 2 µm) which conflicts with data from researchers who have successfully produced silica coated liposomes. Further characterization was not conducted due to poor sample quality. A single Triton X stability assay of cationic liposomes shows definitive degradation at concentration 5% and 10% (v/v) Triton X-100. Future studies will mainly be focused on generating a silica solution without the excess generation of silica particulates. The effects of relative reagent concentration, reaction time, reaction temperature, and pH. More replicates of the Triton X assay will be done to verify the reproducibility of our results. This research was supported in part by NIH Grant R01CA238871 grant, the School of Graduate Studies, and the Rutgers Office for Research and Economic Development.



Endocrine Disruptor Bisphenol A Increases Cell Migration via an Estrogen Receptor Independent Pathway in Triple Negative Breast Cancer

Kyo Chang Lee, Tingying Xie, Cassandra Winz, Nafeesah Scott,
Philip Furmanski, Nanjoo Suh
Rutgers, the State University of New Jersey

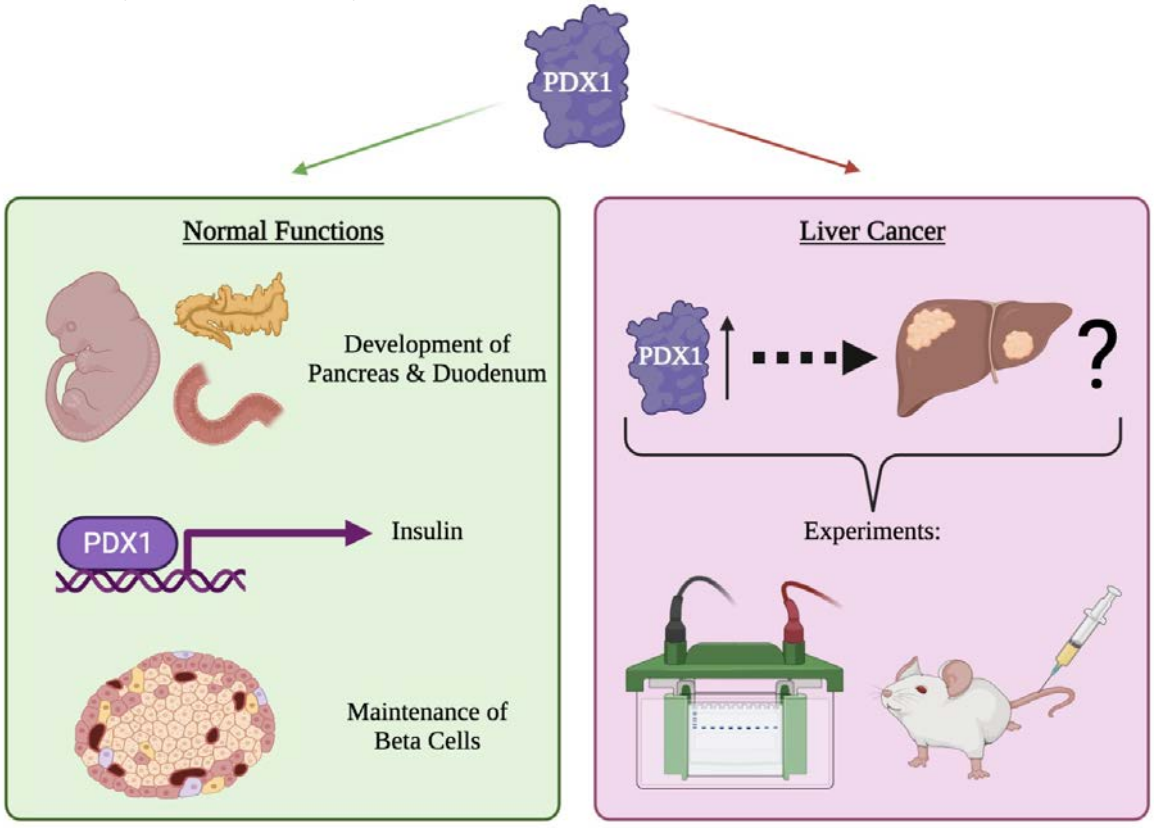
Various endocrine disruptors are suggested to contribute to the development of breast cancer. Bisphenol A (BPA) is one of the endocrine disruptors that is known to be an estrogen receptor (ER) agonist due to structural similarities to the estrogen molecule. BPA has also been reported to bind to receptors other than the estrogen receptor such as estrogen-related receptor γ (ERR γ) and G protein-coupled estrogen receptor (GPER), and activate the estrogen receptor independent pathways in breast cancer cell lines that lack the estrogen receptor. Our goal of this study was to examine whether BPA acts independently from the estrogen receptor, and whether it increases the migration via an estrogen receptor independent pathway. MDA-MB-231 is a triple negative breast cancer cell line lacking ERα, Progesterone Receptor, and HER2, and it is known to have mesenchymal characteristics, including rapid migration in culture. MCF-7 is a cell line that expresses ERα; it has epithelial characteristics, including a slower rate of migration in culture. These cell lines were treated with estrogen (100 pM) and BPA (100 nM and 1 µM) for 1 day. Cell proliferation marker C-MYC was determined by Western blot. The protein level of C-MYC increased in both estrogen and BPA treatments in MCF-7 but not in MDA-MB-231. Cell migration was determined by scratch-wound assays. MCF-7 and MDA-MB-231 were treated with estrogen (100 pM) and BPA (100 nM and 1 µM), and observed for 6 hours to measure the rate of migration. The rate of migration was faster in MCF-7 cells in the presence of estrogen than in its absence. The rate of migration was faster in MDA-MB-231 treated with BPA than in cells treated with estrogen or vehicle control. Our findings suggest that BPA increases the proliferation through ER-mediated action, and that an ER-independent mechanism contributes to the increase in the rate of migration by BPA. Further research is necessary to better understand the estrogen receptor independent actions of BPA involving specific receptors like GPER or ERR γ. Supported by NIH R01 AT007036, R03 CA259650, Busch Biomedical Grant, School of Graduate Studies, the Rutgers Office for Research and Economic Development. and New Jersey Health Foundation.



Insulin Transcription Factor PDX1 Promotes Liver Tumorigenesis

Chacko Jacob, Tinghan Zhao, X. F. Steven Zheng
Rutgers, The State University of New Jersey

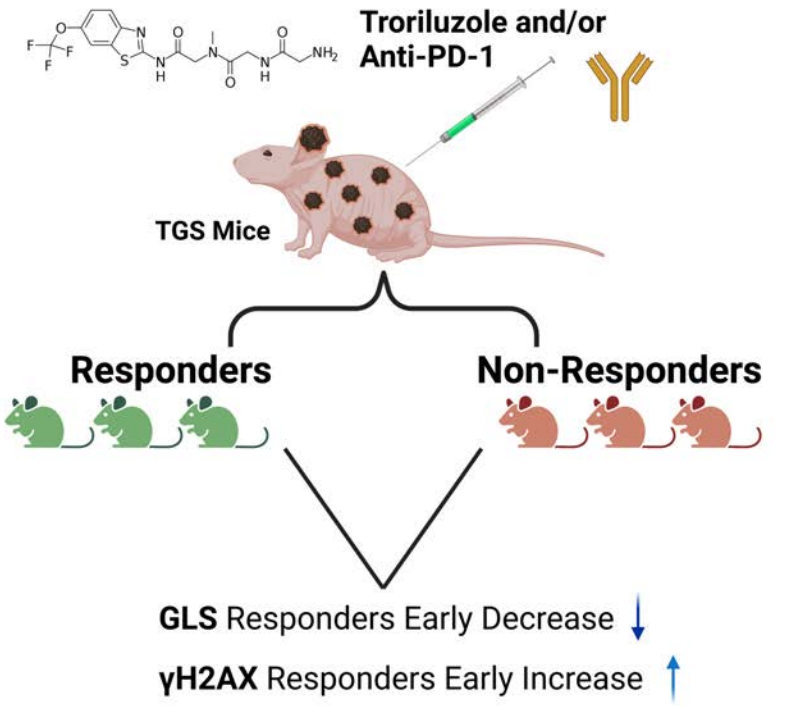
Pancreatic and duodenal homeobox 1 (PDX1) is a protein that is primarily known for its function as an insulin transcription factor. While PDX1 expression is normally restricted to pancreatic beta cells in adult animals, PDX1 has also been found to be expressed in several cancers of non-pancreatic origin, including colorectal, stomach, and liver cancers. However, it is still unclear if and how PDX1 regulates the development of these cancers. The purpose of this study is to determine whether aberrant PDX1 expression promotes liver tumorigenesis. My analysis of liver cancer patient survival data from The Cancer Genome Atlas (TCGA) shows that the survival rate of patients with high PDX1 mRNA expression was significantly decreased compared to that of patients with low PDX1 mRNA expression. To further understand the role of PDX1 in liver tumorigenesis, I performed in vitro and in vivo experiments using cultured liver cancer cell lines and a mouse hydrodynamic transfection (HDT) liver tumor model. Western blot analysis confirms PDX1 expression in liver cancer cell lines, especially in the Huh7 cell line. Furthermore, I ectopically expressed PDX1 in combination with the oncogenes AKT and NRAS in mouse livers through the HDT method. Liver tumor development was observed in the AKT/NRAS/PDX1 group, but not in the AKT/NRAS control group. These results provide evidence for the role of PDX1 in promoting liver tumorigenesis. In the future, I plan to perform more in vitro and in vivo experiments to verify the above results and to investigate the mechanism by which PDX1 drives liver tumorigenesis. Supported by SURF and NIH grants DK124897 and R25ES020721.



Protein Marker Changes as a Result of Glutamatergic Signaling and Immune Checkpoint Inhibition in Melanoma-Prone Transgenic Mice

Mohamad Naser Eddin, Kevinn Eddy, Wasif Rashid, Suzie Chen
Rutgers, The State University of New Jersey

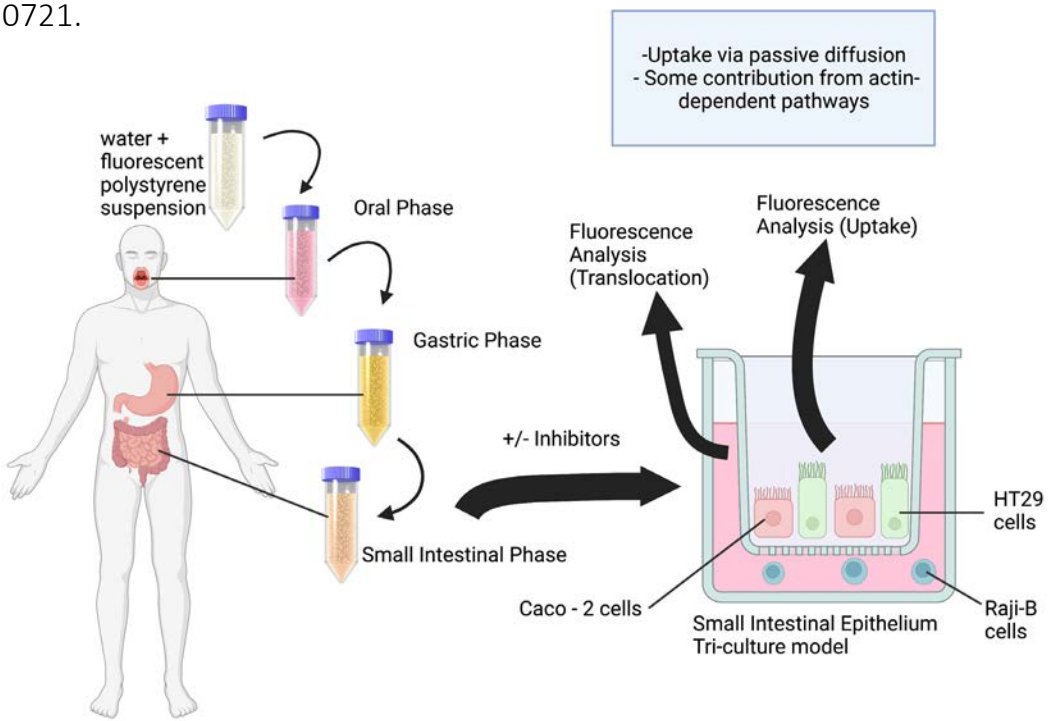
Melanoma, while the least common form of skin cancer, is the deadliest and accounts for the majority of skin cancer mortality. The American Cancer Society estimates that in 2022, approximately 100,000 new cases of invasive melanoma will be diagnosed and 7,650 will result in death. Metastatic melanoma is refractory to many therapies and improvements in therapeutic strategies are essential. The availability of an experimental animal model that recapitulates many of the characteristics in human disorder is a valuable tool in translational research. Our lab has shown that when melanocytes, the pigment-forming cells of the skin, ectopically express a normal neuronal receptor, metabotropic glutamate receptor 1, and activated by its natural ligand, glutamate, leads to cell transformation in vitro and metastatic melanoma formation in vivo. In this study, we have taken excised tumor specimens after the mice have been on treatment for 6, 12, and 18 weeks. Expression of several protein markers were assessed by Western immunoblots to consider for the application as biomarkers to predict treatment outcomes. The protein markers we have selected have been shown by others to be associated with immune evasion, cell metabolism, and DNA damage. At the end of our 18-week longitudinal study the mice were stratified into responders or non-responders based on the RECIST criteria used in human clinical trials. Our preliminary results suggest differential expression profiles between responder and non-responder mice in some treatment modalities and time courses. Complementary assays may further delineate the most suitable biomarkers in therapy prediction. Supported by R25ES020721.



Mechanisms of Micronanoplastic Uptake and Translocation in the Small Intestinal Epithelium by Pathway Inhibition Using a Triculture Model

Faranguisse Sadrieh, Glen DeLoid, Philip Demokritou
Rutgers, The State University of New Jersey

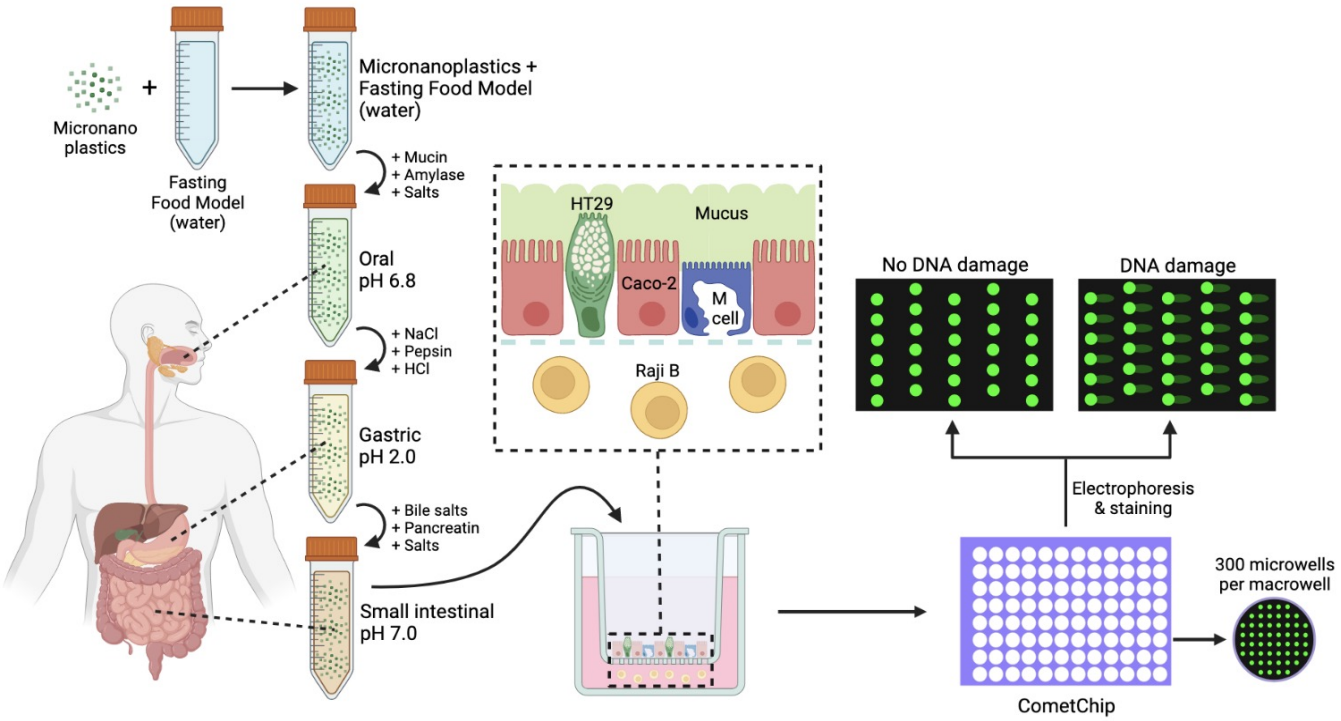
Millions of tons of plastic are produced annually with less than 10% of the amount being recycled, generating large amounts of waste. Micronanoplastics (MNPs) can be defined as small particles of plastics that form by environmental degradation and are considered a serious environmental hazard. Aside from contaminating the environment, MNPs also end up in the human body, raising the need to further study how this impacts human health. In this study, the uptake and translocation of ingested MNPs was assessed using a polysterene model MNP and a triculture small intestinal epithelium (SIE) cellular model coupled with simulated digestions. Several energy dependent pathways are involved in endocytosis and by using certain inhibitors to block these pathways, the micronanoplastic uptake mechanisms can be studied. The inhibitors used for this study are 2-deoxy-D-glucose, sodium azide, chloroquine, dyngo, 7-keto-cholestorol, cytochalasin D, and amiloride, each with varying concentrations. Simulated digestion of the oral, gastric, and small intestinal phases was done with polystyrene MNP at different concentrations to obtain the small intestinal phase digesta. A triculture model which includes enterocytes, HT29 and M-cells cells was treated with the inhibitors and then exposed to the digesta. We allowed for uptake and translocation to occur for 4 hours after which we measured the MNP concentration in the basolateral compartment to determine which pathways were involved with the passage of the MNPs. Following treatment and uptake, the contents within the basolateral and apical compartments of the triculture transwell model were collected and underwent fluorescent analysis to determine MNP concentrations for each pathway treated by the inhibitors. Data showed most uptake was via passive diffusion, with some contribution from actin-dependent pathways (i.e., phagocytosis). Furthers studies utilizing uptake gene siRNA knockdown should be conducted to get more accurate results. Because of the ever-growing threat presented by plastic pollution and wastes, this is an area in critical need for further study. Supported by R25ES020721.



Assessing DNA Damage from Ingested Micronanoplastics

Joshua Baw, Zhening Yang, Glen Deloid, Philip Demokritou
Rutgers, The State University of New Jersey and Harvard University

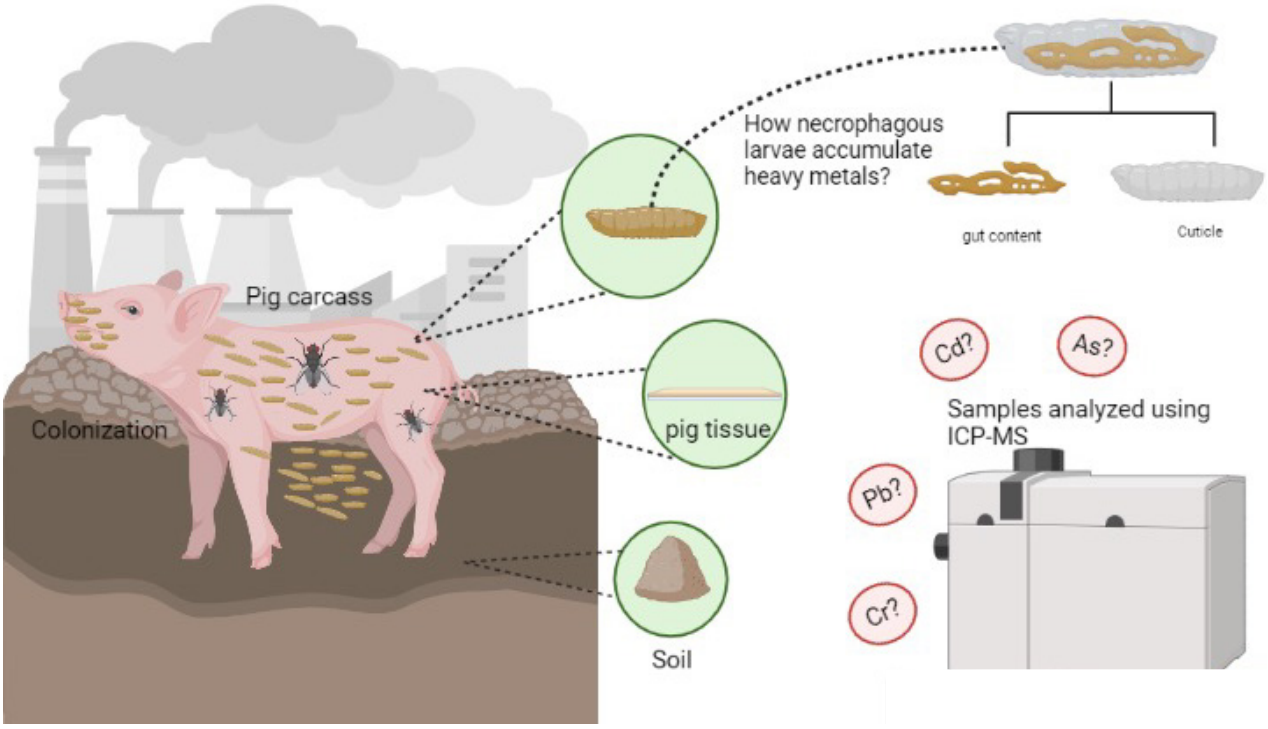
Hundreds of millions of tons of plastic are produced annually, most of which are incinerated in waste plants and degraded in the environment into micronanoplastics (MNPs). MNPs are exposed to animals and humans primarily through ingestion. Thus, studying the health effects of MNPs has become an emerging and crucial research area. However, research on the genotoxicity of MNPs is limited. This study aims to measure the genotoxicity of different types of MNPs using an in vitro triculture small intestinal epithelial model, including Caco-2, HT29, and Raji B cells. Primary 25 and 1000 nm carboxylated polystyrene spheres (PS25C, PS1KC), and secondary incinerated polyethylene (PE-I) MNPs were dispersed in water (fasting food model, FFM) at 0.05, 0.25, and 1.0 mg/mL. To emulate in vivo digestive processes, the suspensions went through oral, gastric, and small intestinal phases of digesta. The cell model was then exposed to MNP-containing small intestinal digesta for 24 and 48 hours. A high-throughput 96-well CometChip platform assessed DNA damage by measuring the average percentage of DNA in the comet tails. Our results showed that 24 and 48-hour MNP exposures induced dose-dependent increases in DNA damage, with statistically significant increases in the 48-hour exposures of 0.25 and 1.0 mg/mL PS 25C compared to the FFM control group ($p < 0.001$). These findings suggest that ingestion exposure to PS 25C may have caused genotoxicity to the triculture small intestinal model and emphasizes the need for further research to evaluate the genotoxicity of MNPs in vivo. Supported by NIH R25ES020721 and the School of Graduate Studies.



Heavy Metal Detection and Quantification on Blow Fly (Diptera: Calliphoridae) Larvae and Potential Forensic Entomotoxicology Applications

Daniela Bermeo Grajales, Cathleen Doherty, Denise Gemmellaro
Rutgers, The State University of New Jersey and Kean University

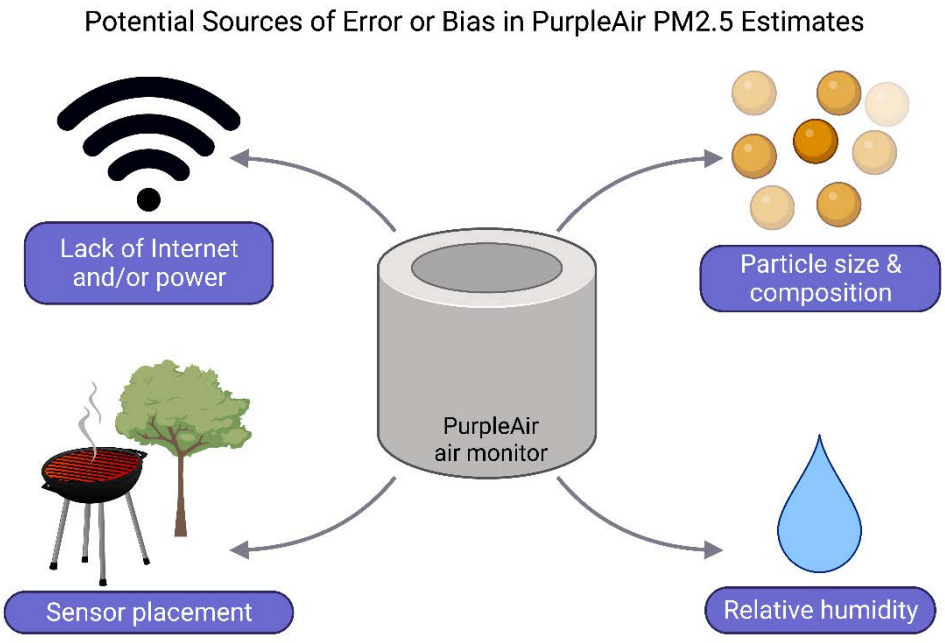
Insects are quite cosmopolitan and are exposed to a wide range of biotic and abiotic conditions. These conditions may result in insects accumulating xenobiotics present in their food and environment. Blow flies (Diptera: Calliphoridae) will colonize and start feed on corpses shortly after death; because of this, they are often used to estimate the minimum post-mortem interval (mPMI). Forensic entomotoxicology focuses on the use of insects to identify xenobiotics which may have been present in the corpse; these substances can also have an influence on the developmental time of the insects and consequently, this can have an impact on the estimation of mPMI. Heavy metals are toxic and non-biodegradable elements and their presence in the environment can be used to indicate health risk for all exposed living organisms. The objective of this study was to develop a protocol for the detection and quantification of heavy metals in Calliphoridae larvae. Metal accumulation and distribution was analyzed in the gut content and cuticle of the larvae; these were compared to the heavy metals detected in tissue samples of the carcass and in the soil. The results represent a first step towards a more structured protocol for the analysis of heavy metals from insects and towards a better understanding of how calliphorids accumulate metals. Future work will assess the influence of heavy metal levels and larval growth and will refine the way that Calliphoridae can be used in forensic entomotoxicology investigations. Supported by the SOT Intern Program, EMSOP, and NIH R25ES020721.



Use of Low-Cost Air Monitors to Measure Particulate Matter 2.5 Pollution in a NJ Community

Betia Zeng, Fatima Haynes, Robert Laumbach
Rutgers, The State University of New Jersey

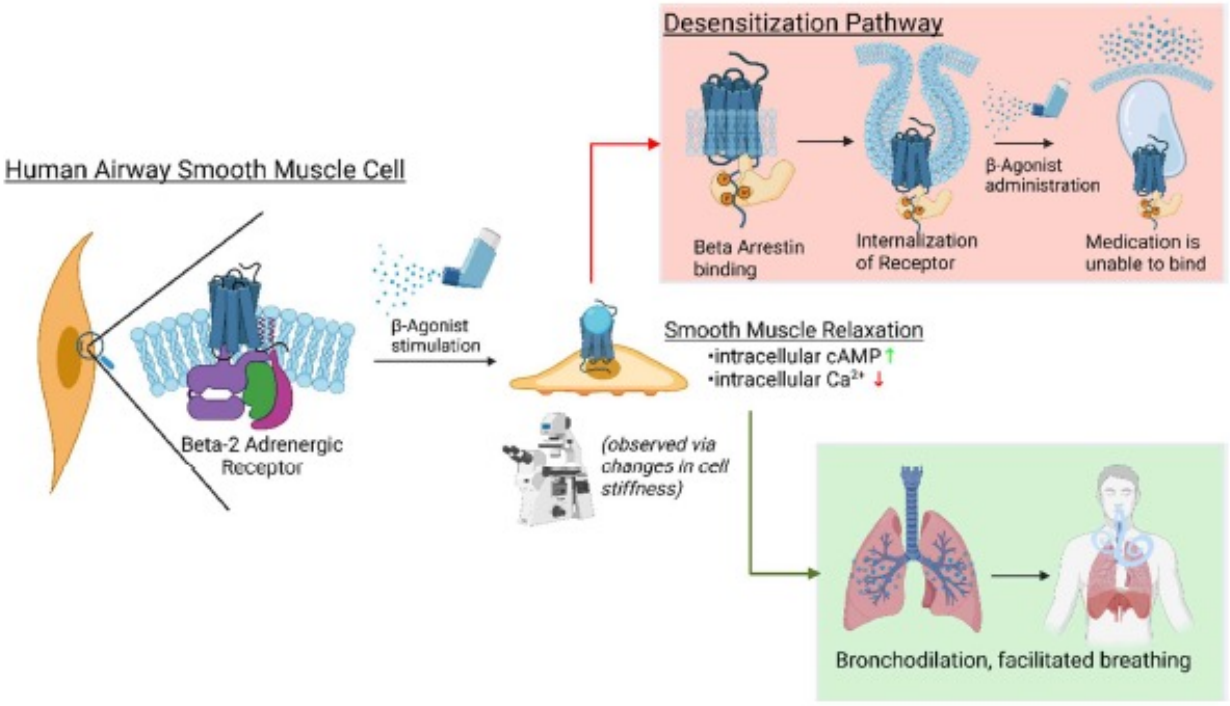
PM2.5, or particulate matter with an aerodynamic diameter < 2.5 µm, is a regional air pollutant that has been linked to multiple adverse health effects including the exacerbation of asthma. In urban communities such as Elizabeth NJ, where traffic is a major source of PM2.5 and asthma is prevalent, community scientists are leading the way in making air pollution data more accessible. Groundwork Elizabeth, a local community organization that aims to reduce the impacts of environmental pollutants, partnered with Rutgers EOHSI to evaluate the accuracy and reliability of low cost PurpleAir monitors in measuring PM2.5 concentrations in Elizabeth, NJ. PurpleAir monitors are low-cost air quality monitors that allow communities to measure PM2.5 concentrations and view and share data in real time online. However, PurpleAir monitors tend to overestimate PM2.5 concentrations and are also subject to loss of data without reliable internet access, leading to validity concerns. We collocated three PurpleAir monitors with a NJ Department of Environmental Protection (NJDEP) reference monitor over a 2-week period. We used a linear regression model to develop a calibration equation based on the collocation. After placing the monitors in Elizabeth, NJ for a 3-week period, the calibration equation was used to correct the community PM2.5 concentrations, which were then compared to the central site reference monitor measurements. The correction increased agreement of PurpleAir measurements with reference measurements. The R-squared ranged from 0.636 to 0.663 and varied according to each monitor. The average slope prior to correction was 1.535 while the average slope after correction was 0.984. PurpleAir monitoring systems can be a reliable, inexpensive method for communities to estimate ambient PM2.5 levels if the data are appropriately adjusted prior to interpretation. Supported by R25ES020721.



Modeling and Modulating the Functional Desensitization of β2AR in Real-Time

Justin Lee, Jordan Lee, Steven An
Rutgers, The State University of New Jersey

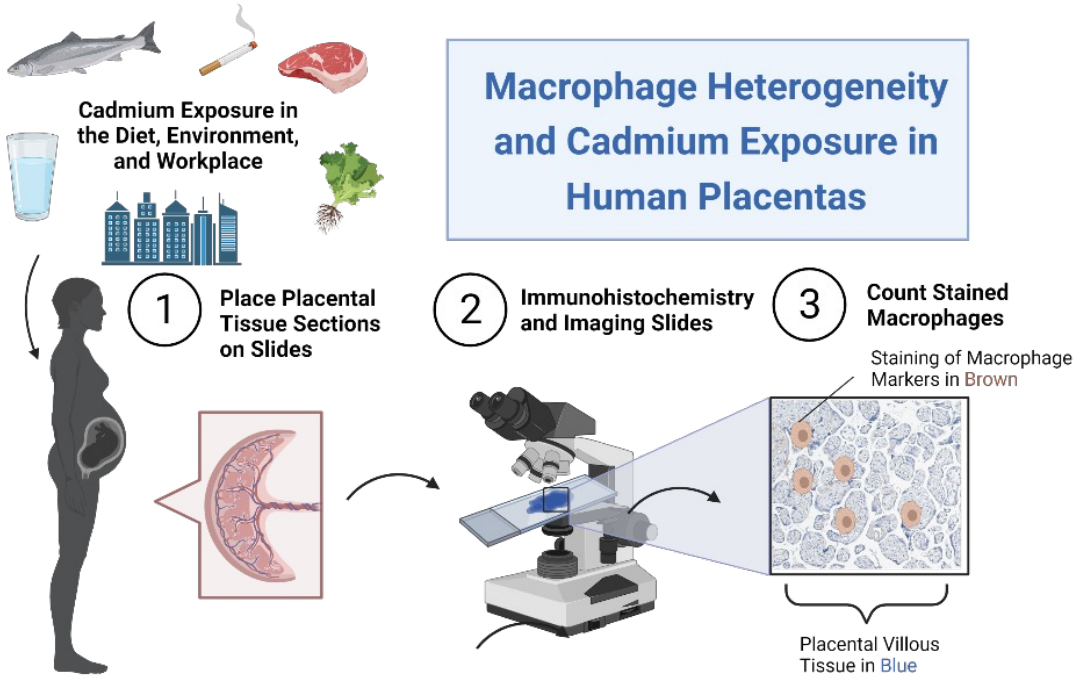
Desensitization of the beta-2 adrenoceptor (β2AR) is a phenomenon associated with prolonged or repeated exposure to beta-agonists, contributing to increased morbidity and decreased quality of life for asthma patients. Stimulation of the β2AR by Gαs-agonists triggers Gαs-mediated activation of adenylyl cyclase, which converts ATP to cAMP, ultimately triggering smooth muscle relaxation. Betaarrestin binding is a homeostatic mechanism to desensitize and internalize β2AR via endocytosis. The purpose of this study was to develop a new experimental paradigm to detect, in real-time, functional desensitization of β2AR expressed on human airway smooth muscle cells. We used an RGD-coated ferrimagnetic microbead functionalized to the cytoskeleton through cell surface integrin receptors and measured the dynamic changes in cytoskeletal stiffness of human airway smooth muscle cells in response to the β-agonist isoproterenol via magnetic twisting cytometry (MTC). We observed a 32% loss of cell relaxation as soon as 20 minutes after stimulation with isoproterenol, which we believe to be the observable impact of β2AR desensitization. We verified this assumption through experimentation with isobutylmethylxanthine (IBMX), a wide-ranging phosphodiesterase inhibitor. Observing a loss of relaxation from cells pretreated with IBMX, we concluded that loss of cell relaxation was not solely due to the backdoor mechanism of cAMP breakdown by phosphodiesterases. In one IBMX-pretreated cell line, we observed 100% loss of isoproterenolinduced relaxation within 30 minutes, thus suggesting functional β2AR desensitization. Using MTC, we observed that the desensitization-driven wane of cell relaxation occurs rapidly and determined that the breakdown of cAMP by phosphodiesterases was not the sole cause of the loss of relaxation. Supported by R25ES020721.



Macrophage Heterogeneity and Cadmium Exposure in Human Placentas

Shine Wang, Lauren Walker, Ranran Zhang, Cathleen Doherty,
Carol R. Gardner, Debra L. Laskin, Lauren M. Aleksunes
Rutgers, The State University of New Jersey

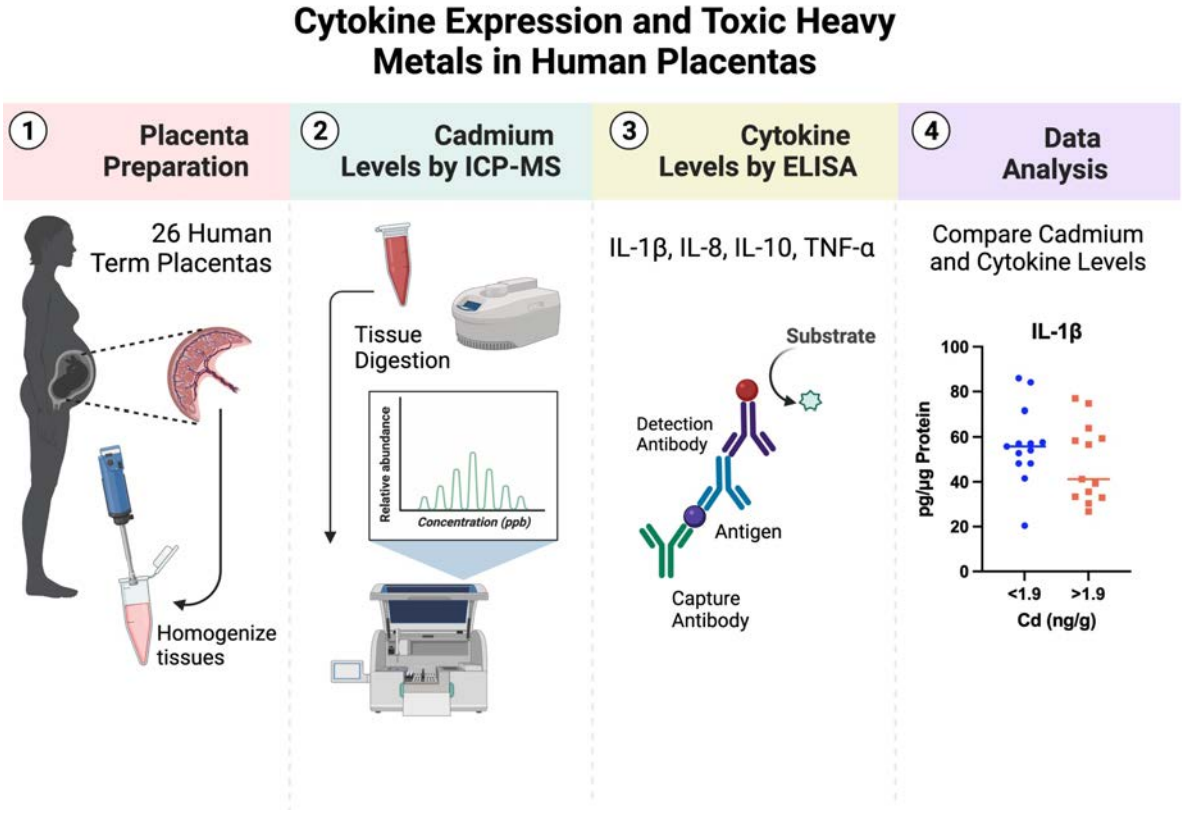
Placental macrophages protect the mother and fetus from infection by engulfing harmful bacteria and signaling with other cells. Cadmium (Cd) is a prevalent heavy metal environmental pollutant that targets the placenta and interferes with normal functioning and has been shown to disrupt immune signaling in other tissues. We sought to evaluate associations between enrichment of macrophage subpopulations in human placentas and accumulation of Cd. Healthy full-term human placentas (n=20) were collected from Robert Wood Johnson University Hospital. Cd concentrations were quantified using ICP-MS. Tissues were designated as low (N=10) or high Cd (N=10) if concentrations were below or above the median level of 2.9 ppb, respectively. Placental tissue sections were stained for macrophage markers CD14, CD68, CD163, CD206, and DC-SIGN using immunohistochemistry and imaged with GRYPHAX software. The number of positively stained cells were counted manually using ImageJ's Cell Count software and normalized to tissue area. No differences in placental weight were observed between low and high Cd exposure; however, birth weight tended to be reduced in placentas with high Cd levels (p=0.0887). Notably, the number of macrophages that stained for the scavenger receptor (CD163) was increased (44%) (p=0.0014), while enrichment of macrophages stained for the mannose receptor (CD206) was reduced (p=0.0438) in placentas with cadmium levels over 2.9 ppb. Notably, CD163 is a homeostatic receptor and increases in the placenta has been linked with obesity, preeclampsia, and gestational diabetes. By comparison, CD206 is a pathogen recognition marker, and its staining is reduced in placentas from pregnancies with spontaneous preterm birth. As a result, placentas with higher Cd levels may be more susceptible to pathogenic infections and pregnancy complications. This work was supported through the ASPET SURF Program, Rutgers Office for Research and Economic Development, and NIH grants R25ES020721 and R01ES029275.



Cytokine Expression and Toxic Heavy Metals in Human Placentas

Faythe Cooper, Lauren M. Walker, Kim Bodenlos, Devika Sachdev,
Cathleen Doherty, Lauren M. Aleksunes
Oberlin College and Rutgers, The State University of New Jersey

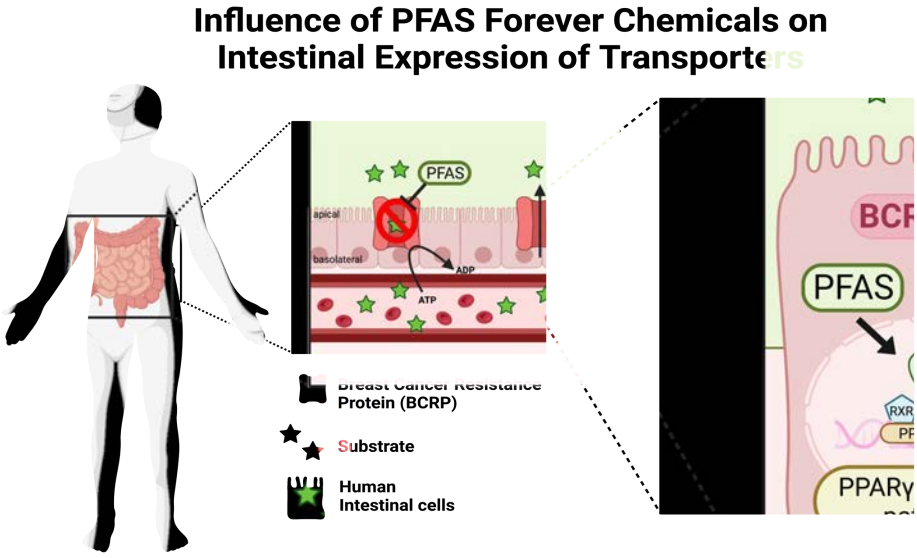
Cadmium (Cd) exposure has been associated with pregnancy complications such as preterm birth and pre-eclampsia. Understanding the cellular mechanisms involved in Cd exposure can shed light on the effects of metal contaminants on placental function. We speculate that Cd could alter inflammatory signaling in the placental immune system and inform potential therapeutic targets to improve the health of pregnant women. For this purpose, we sought to investigate the relationship between cadmium accumulation in human placentas and the expression of four cytokines (Interleukin-1β, IL-1β; Interleukin-8, IL-8; Interleukin-10, IL-10; and Tumor Necrosis Factor-α, TNF-α). Healthy term human placental biospecimens (N=26) were collected at birth. Cd content was assessed using inductively coupled plasma mass spectrometry and cytokine expression was measured using enzyme-linked immunosorbent assays. The median Cd level in the human placentas was 1.9 ppb (range 0.7-6.4 ppb). Placenta samples were divided into a higher Cd content group (N=13) and a lower Cd content group (N=13) based on the median Cd concentration. Levels of pro-inflammatory cytokine expression were compared between placentas with <1.9 versus >1.9 ppb cadmium using t-tests. and no differences were observed: IL-8 (p=0.38), IL-1β (p=0.24), IL-10 (p=0.30), and TNF-α (p=0.29). In a healthy population, relationships between Cd accumulation in the placenta and enrichment of cytokines were not observed. Future studies may include placentas from pathologic pregnancies or with a greater range of Cd exposures. Overall, a comprehensive understanding of such mechanisms can contribute to improvements in maternal health. This work was supported by the SOT Intern Program, EMSOP, and NIH grants R25ES020721 and R01ES029275.



Effect of Perfluorinated “Forever” Chemicals on the Expression of Intestinal Xenobiotic Transporters

Ruth Meletz, Xia Wen, Lauren M. Aleksunes
University of California, Riverside and Rutgers, The State University of New Jersey

A class of synthetic chemicals, perfluorinated and polyfluorinated substances (PFAS), have been used for decades in non-stick cookware, fire-fighting foams, textiles, packaging, and cosmetics. PFAS are found in almost the entire U.S population and elevated concentrations may contribute to the development of chronic conditions including hyperuricemia and hypercholesterolemia. Prior studies have demonstrated that PFAS can inhibit the functional activity of the intestinal uric acid transporter, breast cancer resistance protein (BCRP/ABCG2), which may explain a mechanism for increased risk of hyperuricemia. In the current study, we sought to determine whether PFAS chemicals alter expression of BCRP in human intestinal cells. Pharmacological agonists of the AhR (β-napthoflavone (β-NF) and PPARγ transcription factors (rosiglitazone, (RG) were used as positive controls that induce BCRP in human Caco-2 cells, a well-studied model of the intestinal barrier. Caco-2 cells were treated with vehicle (0.5% DMSO), various PFAS chemicals (10μM, 50μM), or β-NF/RG (25μM, 100μM) for 72 hours. No cytotoxicity was observed at these concentrations. BCRP expression was semi-quantified using SDS-PAGE and Western blot analysis. As expected, β-NF and RG induced BCRP expression. By comparison, at concentrations of 10μM, PFAS chemicals did not significantly change BCRP expression. Ongoing studies with PFAS treatments at 50μM are being conducted to determine whether PFAS is able to change BCRP expression at higher concentrations. These studies will advance understanding of the interplay of PFAS and BCRP and the risk of developing hyperuricemia in individuals exposed to PFAS. This work was supported by the SOT Intern Program, EMSOP, NIH grants R25ES020721 and R01ES029275, and MARC U T34GM062756.



The Impact of Maternal Diet on Flame Retardant Related Gene Expression in Neonatal Mice

Zachary A. Kobs, Samantha Adams, Shabree Anthony, Ali Yasrebi,
Lauren Aleksunes, Troy A. Roepke
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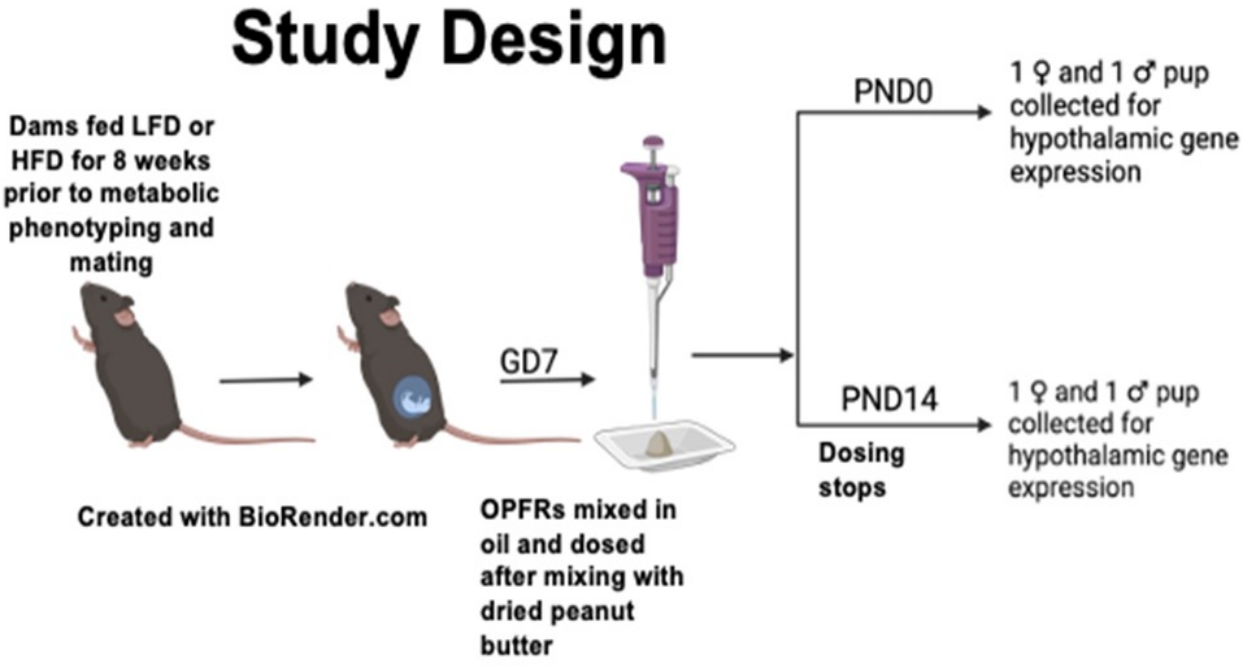
The prevalence of the obesity epidemic and the ubiquity of endocrine disrupting chemicals (EDC) produces a unique problem for pregnant individuals. This is because interactions of maternal obesity and EDC exposure on developmental programming in the offspring, at the hypothalamic level, may lead to obesity and other metabolic disorders. The specific aim of this project is to determine the effects of maternal obesity on the neonatal expression of Blood Brain Barrier (BBB) genes following organophosphate flame retardants (OPFR) exposure. We conducted our experiment by feeding 10 WT females a low-fat diet (10% fat, LFD) and 10 WT females a high-fat diet (45% fat, HFD) for 8 weeks prior to mating. Once mating occurred all females were dosed with OPFRs from GD7 to PND14. At PND0 and PND14, the mediobasal hypothalamus from 1 female and 1 male pup from each litter were collected for analysis of gene expression. RNA was extracted and samples were prepared for quantitative real-time PCR. Our results suggest that genes associated with the BBB were not affected by maternal diet in the PND0 and PND14 cohorts. However, expression of CLDN1 and OCLN were different between the sexes at PND14. Other genes involved in reproduction and energy balance were altered by maternal HFD in the neonates and juveniles. Ongoing studies are characterizing the permeability of the BBB in littermates and characterizing the metabolic and behavioral effects in adult littermates. These results help us understand how maternal obesity interacts with OPFR exposure on the development of fetus and neonatal brains. Future direction will examine the hypothalamic and hepatic transcriptome in offspring from lean and obese dams with or without OPFR exposure. Supported by the SOT Intern and MARC Programs and EMSOP.



Orexin 1 Receptor Antagonist SB-334876 Impairs Sustained Attention but Only at High, Non-Clinically Relevant Doses

Nivedita Krishnakumar, Morgan Paladino, Joost Wiserke, Audrey Asare, Shuchi Merai, Shayna O'Connor, Michelle Billoti, Kuba Suchojad, Morgan H. James
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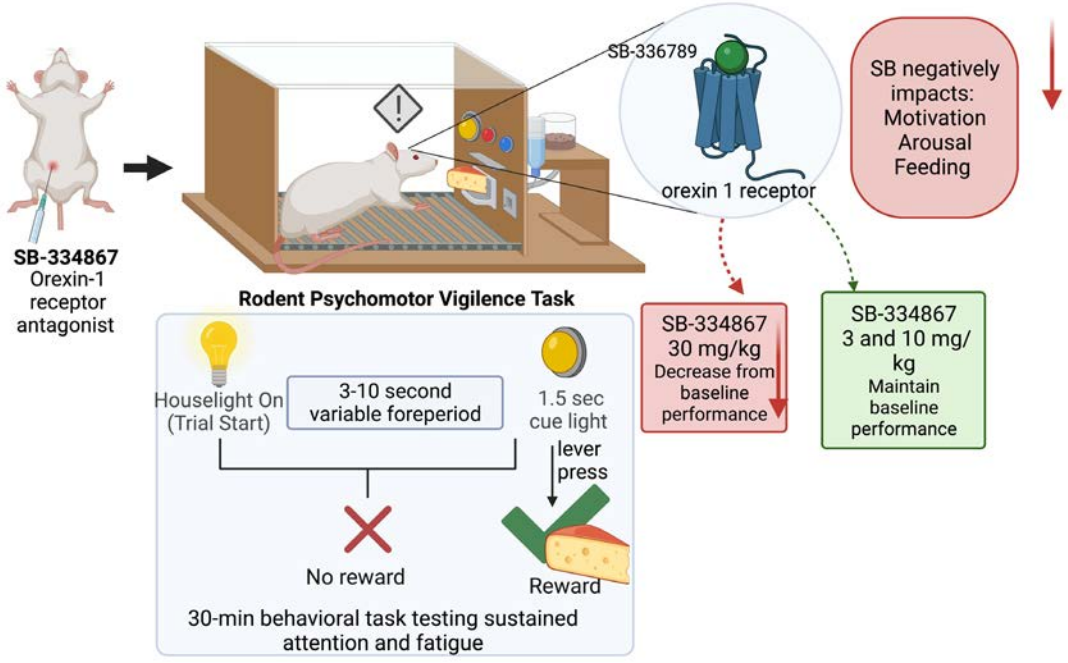
The hypothalamic orexin (hypocretin) system affects psychological functions such as arousal, wakefulness, motivation, and sleep. Due to its influence in motivation, orexin-1 receptor antagonist SB-334876 shows promise as a therapeutic for substance use disorder due to its effect in suppressing drug seeking behavior. Knowing the role of OxR1 signaling in cue-driven motivation, we wanted to determine SB-334876's effect on sustained attention using the rodent psychomotor vigilance task. The 30 min operant chamber task, "rPVT '' measures changes in sustained attention and fatigue with parameters such as performance accuracy, motor speed, premature responding, and lapses in attention. We validated the ability of rPVT task by modulating norepinephrine signaling with amphetamine, guanfacine, and atipamezole to be able to produce bidirectional attention modulation effects. Once it was determined rPVT can assess sustained attention we investigated the effects of orexin-1 receptor antagonist SB-334876 on this paradigm. Results showed a dose dependent effect with atipamezole, guanfacine, and amphetamine where the larger dose showed a decrease in performance while the moderate dose showed a slight increase and lowest stayed at baseline. This effect was apparent when looking at accuracy and reaction time. Looking at SB, we see a prominent decrease in performance and sustained attention in the highest dose, 30 mg/kg, whereas the low and moderate doses stayed at baseline. With these results, it can be concluded that SB-334876 orexin 1 receptor antagonist can be a promising therapeutic to suppress drug seeking behavior because it does not have a significant impact on sustained attention in clinically relevant dosage (3 and 10 mg/kg). Supported by NIH Grants R00DA045765 and R25ES020721.



Determining if a Novel CRISPR Enzyme Can Efficiently Induce Deletions of Hexanucleotide G4C2 Repeat Mutations in the ALS Gene C9ORF 72 *In Vitro*

Daniel Luo, Ian O'Connor, Omer Abdel Wahab, Renping Zhou
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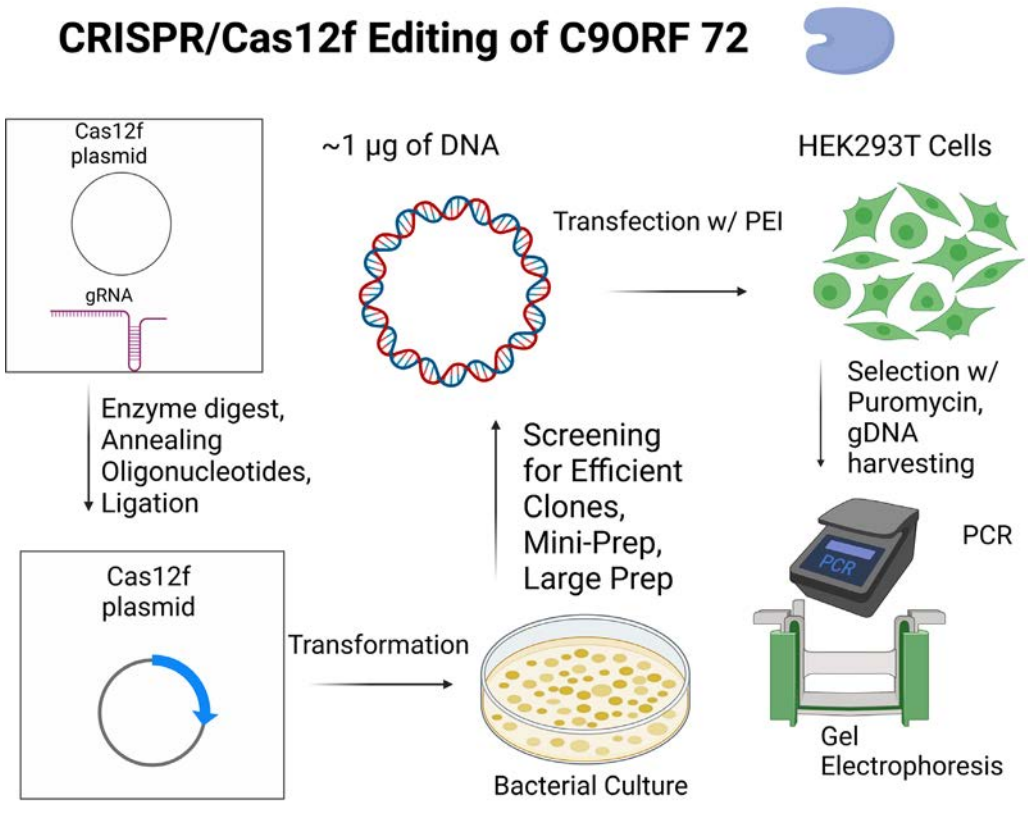
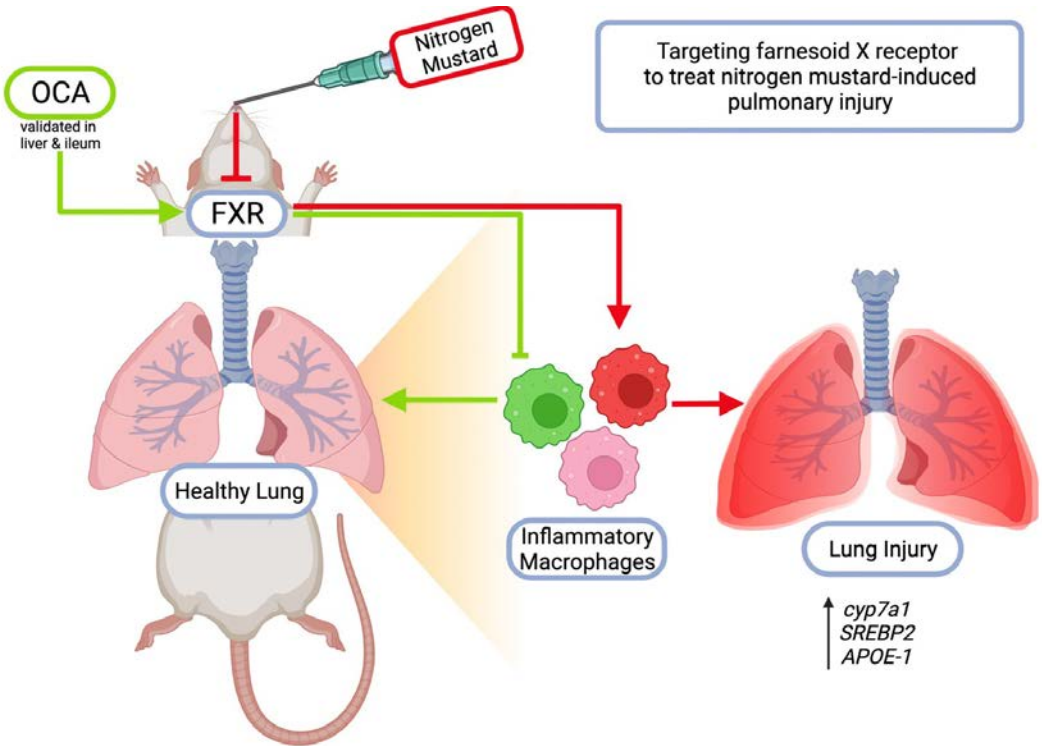
CRISPR technology utilizes the enzyme Cas 9 from various bacteria to act an efficient endonuclease in inducing deletions and NHEJ of DNA. However, AAVs can only package ~ 4.7 kb of DNA, and the DNA required to produce Cas9 is greater than 4.7 kb. Cas 12f, a smaller Cas enzyme, can fit in AAV vectors. In this study, we sought to determine if Cas12f can efficiently induce deletions of G4C2 Repeat Mutations in the ALS Gene C9ORF 72 *in vitro.* Plasmids containing the DNA for Cas12f production were digested by restriction enzyme and then purified, and gRNA polynucleotide sequences were ligated to the leftover backbone of the plasmid. Bacterial cells were then transformed utilizing the new plasmid, cultured and then the plasmid DNA was harvested utilizing Qiagen Mini-Prep and Large-Prep kits. HEK293T cells were then transfected with various gRNA and Cas 12f pairings. gDNA (genomic DNA) was then harvested from the cells and amplified utilizing PCR. Gels were run to observe any editing from the wild type. Simultaneously, another plate of the same HEK293T cells were being selected with Puromycin, and the selected HEK293T cells underwent the same procedures as above. The significance of this study is that if Cas12f is efficient in producing deletions, that gene therapy clinical trials utilizing AAVs could be more efficient. The study is still ongoing, so future experiments include comparing Cas9 and Cas12f efficiencies, mRNA deliveries of Cas12f, and/or different methods of delivering Cas12f DNA such as using lipid nanoparticles. Supported by R25ES020721 and the Rutgers Office for Research and Economic Development.



Farnesoid X Receptor: A Novel Therapeutic Target for Nitrogen Mustard-Induced Pulmonary Injury

Rachel Sun, Jaclynn Andres, Kinal Vayas, Jordan Lee, Grace Guo,
Andrew Gow, Jefferey Laskin, Debra Laskin
Rutgers, The State University of New Jersey

Nitrogen mustard (NM; (bis(2-chloroethyl)methylamine) is a cytotoxic alkylating agent that causes macrophage-mediated inflammatory disease that can progress to fibrosis. The nuclear receptor – farnesoid X receptor (FXR) – regulates lipid homeostasis and exhibits anti-inflammatory characteristics. We hypothesize that activation of FXR will reduce macrophage-mediated inflammation and prevent the development of fibrosis following NM exposure. Male Wistar rats were exposed to phosphate-buffered saline (CTL) or NM (0.125 mg/kg) via *i.t.* Pencentury Microsprayer™ aerosolization followed by oral administration of the FXR-agonist obeticholic acid (OCA) or vehicle control (peanut butter, 0.13-0.18 g), 1x/ day, 5 days/week. Lung, liver, ileum, and alveolar macrophages were collected 28d post-exposure. Initially, we assessed the effects of OCA on FXR activity by evaluating mRNA expression of the FXR target genes in the liver (*cyp7A1, BSEP, FXR*) and ileum (*SHP-1, FGF15*, *FXR*). OCA administration increased *FXR*, *BSEP, FGF15*, and *SHP*, but decreased *cyp7A1* expression when compared to vehicle control. Next, we assessed the FXR pathway in lung macrophages by analyzing mRNA expression of target genes. We found that NM significant upregulated *cyp7A1*, *SREBP2*, and *APOE-1* indicating an inhibition of FXR activity; OCA significantly reduced this response. To determine whether this blunted NM toxicity, we evaluated the effects of OCA activity on NM-induced structural alterations in the lung. Exposure of rats to NM caused pulmonary edema, thickening of the epithelium, and circularization of alveoli. This was blunted by OCA. Taken together, these data demonstrates that FXR plays a central role in regulating NM-induced pulmonary injury and provides a potential target for the development of drugs to treat mustard poisoning. Supported by NIH grants AR055073, R25ES020721, and ES005022.



Pulmonary Exposure to Nitrogen Mustard Induced Damage to Small Intestines in Rats

Olympia Su, Jaclynn A. Meshanni, Isabel M. Parzecki, Alexander M. Donlon, Peihong Zhou, Debra L. Laskin, Jeffrey D. Laskin, Laurie B. Joseph
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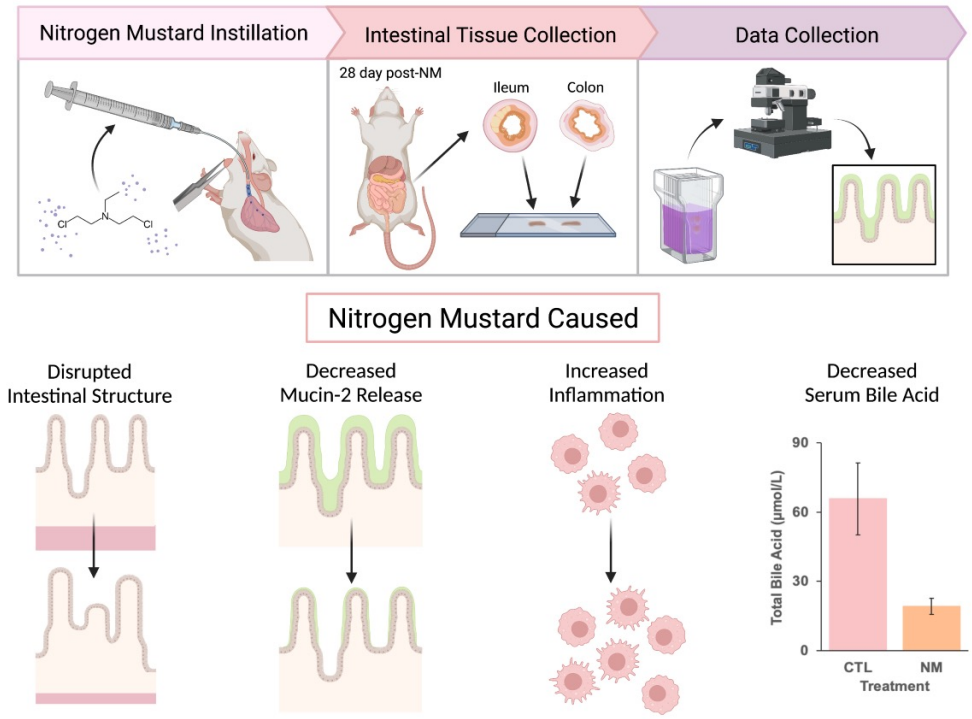
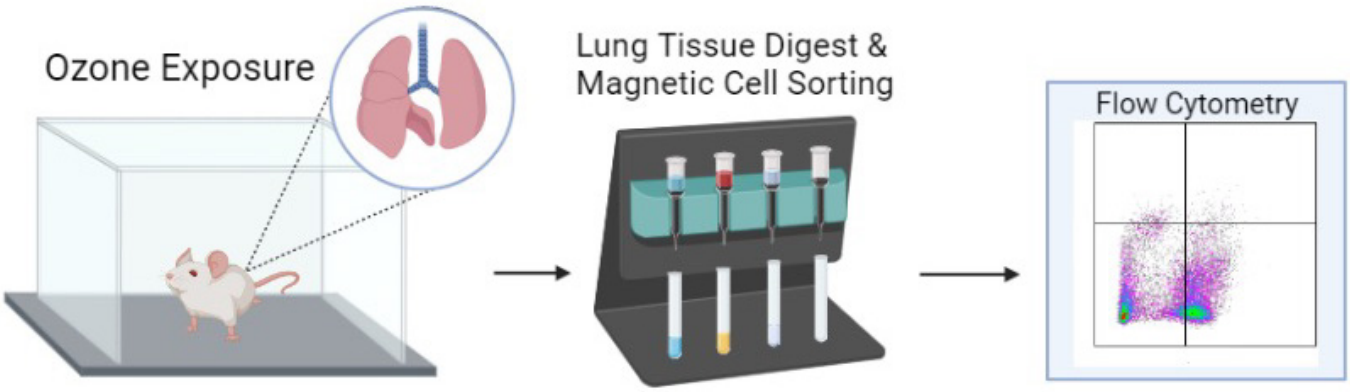
Gastrointestinal toxicity (GI) is a characteristic response of humans to mustard vesicants, regardless of the exposure route. In present studies, we characterized GI toxicity in Wistar rats following pulmonary exposure to nitrogen mustard (NM). Rats were euthanized 28 d after exposure to aerosolized NM (0.125 mg/kg) or phosphate buffer saline (control). NM caused significant damage to the ileum including inflammation, ulceration, and blunting of villi which was adjacent to a thinned submucosa. A significant decrease in the thickness of the muscularis externa was also observed in the ileal structure (66.6 ± 4.5 µm in control and 50.4 ± 2.5 µm in NM). Mucin-2, a gel-forming glycoprotein released from goblet cells essential for epithelial protection, was expressed in the crypts of control and released into the interstitial space. NM suppressed mucin-2 release into the interstitial space. F4/80, a murine monocyte-macrophage marker indicative of inflammation, increased following NM exposure in ileum compared to control. Serum bile acids, which are known to exert hormone-like functions via activation of nuclear and membrane-bound receptors, can modulate intestinal integrity and immunity, were found to be markedly reduced in NM animals (65.73 ± 15.65 µMol/L in control and 19.19 ± 3.51 µMol/L in NM). These data demonstrate that NM causes damage to the ileal villi and crypts. Combined with alterations in bile acid homeostasis, this likely impacts normal intestinal function. Further studies will investigate mechanisms of NM damage, 3 day post-NM exposure damage, and the use of synthetic bile acid, obeticholic acid, in mitigating NM injury in rat intestines. Supported by NIH U54AR055073 and R25ES020721.



PGC-1β Regulates Inflammatory Macrophage Recruitment after Ozone Inhalation in Mice

Benjamin Gelfand, Cody Smith, Debra Laskin
Rutgers, The State University of New Jersey

Ozone is a ubiquitous urban air pollutant that causes airway inflammation and hyperresponsiveness in both healthy and susceptible populations. Inflammatory macrophages play a key role in ozone-induced lung injury by regulating the acute initiation and later resolution phases of the inflammatory response. These distinct activities are mediated by subpopulations broadly classified as M1/pro-inflammatory and M2/anti-inflammatory which sequentially accumulate in injured tissues. Proper control of the inflammatory response requires a balance between M1 and M2 activity. The transcriptional coactivator PPARγ coactivator-1 β (PGC-1β) modulates the activity of transcription factors involved in M2 activation. We hypothesized that PGC-1β signaling attenuates ozone-induced lung injury by promoting M2 phenotype and resolution of inflammation. For these studies, we utilized a conditional Cre-lox mouse model in which PGC-1β is specifically knocked out in CX3CR1+ macrophages (PGC-1β KO). Wild-type and PGC-1β KO mice were exposed to air or ozone (0.8 ppm, 3 hr) and euthanized 72 hours post-exposure. $CX3CR1^+$ cells were enriched from lung tissue digests by magnetic activated cell sorting and specificity of knockdown confirmed by western blot for PGC-1β in $CX3CR^+$ and $CX3CR1^-$ populations. Phenotypes of $CX3CR1^+$ cells were then characterized using techniques in flow cytometry; results revealed that the majority of $CX3CR1^+$ cells were Siglec-F^+/$CD11c^+$ alveolar macrophages (69.2%) and Siglec-F^-/$CD11b^+$ inflammatory macrophages (28.5%). We observed an increase in the number of inflammatory macrophages in both male and female wild-type mice exposed to ozone compared to air controls; this response was diminished in male and female PGC-1β KO mice. We then performed immunohistochemical (IHC) staining of CD11b in lung tissue sections; efforts to semi-quantitate CD11b staining are currently underway. In conclusion, we confirmed that PGC-1β is specifically deleted in $CX3CR1^+$ macrophages, and that these are predominantly resident alveolar and to a lesser extent, inflammatory macrophages. Furthermore, these results suggest that knockdown of PGC-1β impairs recruitment of inflammatory macrophages. Future studies should investigate the mechanism by which PGC-1β regulates inflammatory macrophage recruitment and how this influences ozone-induced lung injury. Supported by R01ES004738, F32ES030984, K99ES032473, R25ES020721, and the ASPET SURF Program.



Nitrogen Mustard Exposure Upregulates PCNA Expression in Mouse Precision Cut Lung Slices

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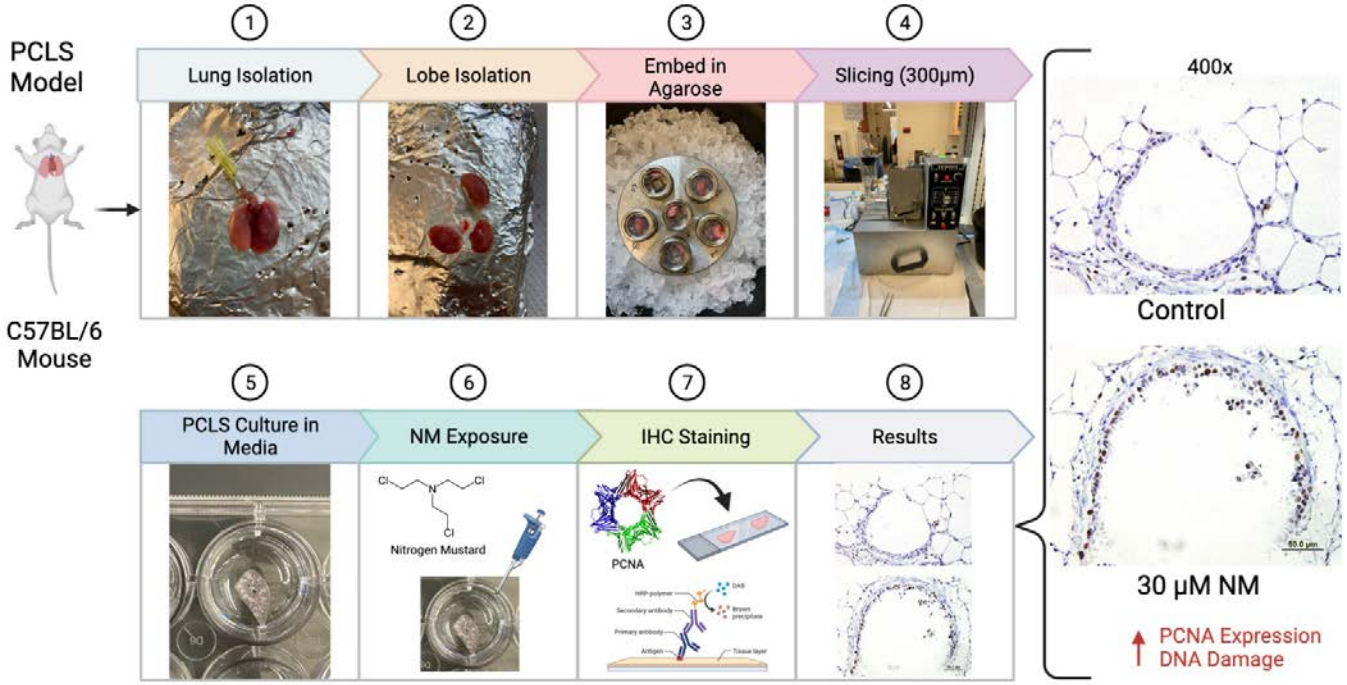
Jefferey Laskin, Debra Laskin
Rutgers, The State University of New Jersey

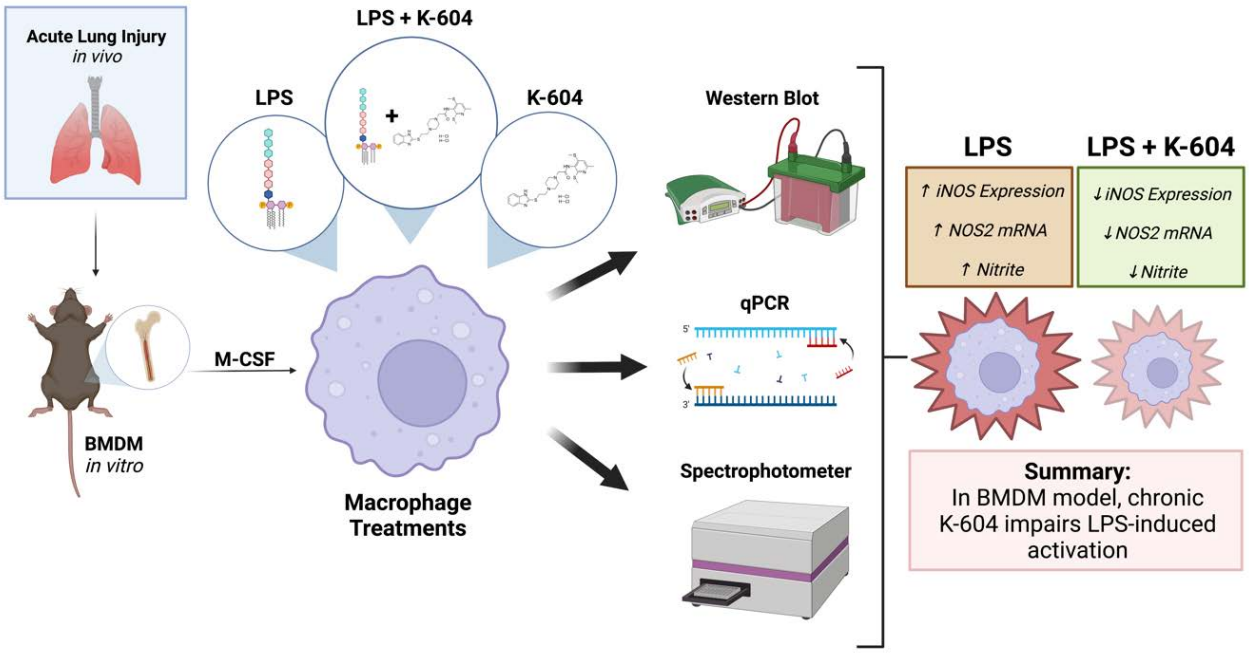
Nitrogen mustard (NM) is a bifunctional alkylating agent that causes acute injury to the respiratory tract leading to fibrosis. In these studies, precision cut lung slices (PCLS) were used to assess initiating events in NM lung toxicity. PCLS are comprised of parenchyma and all resident cells within the lung. Proliferating cell nuclear antigen (PCNA) is a marker of DNA replication and repair. Increases in expression of PCNA is considered an indicator of DNA damage caused by toxicant exposure. In this study, PCNA expression was assessed in PCLS after NM exposure. C57BL/6 mice were euthanized, tracheotomized and the lungs filled with agarose. Lung lobes were isolated and 300 µm thickness PCLS prepared using a Krumdieck Tissue Slicer. PCLS were washed twice with culture media and incubated for 24 hours. PCLS were then exposed to 30 µM NM or culture media (control) for 1 hour. After 24 hours PCLS were fixed with formalin, embedded in paraffin, and sectioned for immunohistochemistry. Non-specific antigen binding sites in the tissue was blocked by incubation of the PCLS with serum for 2 hours; this was followed by overnight incubation at 4ºC with anti-PCNA antibody. Visualization of antibody binding was performed using a Vectastain kit and diaminobenzidine. Qualitative analysis of images revealed greater expression of PCNA in airways of lung slices exposed to NM compared to control. Increased levels of PCNA expression indicate initiation of tissue repair mechanisms after NM-induced DNA damage. Further studies will investigate signaling pathways regulating tissue repair. Supported by NIH Grants AR055073, R25ES020721, and the ASPET SURF Program.



Acat-1 Inhibition Limits iNOS in an *In Vitro* Model of Macrophage Activation

Sung Jae Lee, Emily Stevenson, Elena Abramova, Changjiang Guo, Andrew Gow
Rutgers, The State University of New Jersey

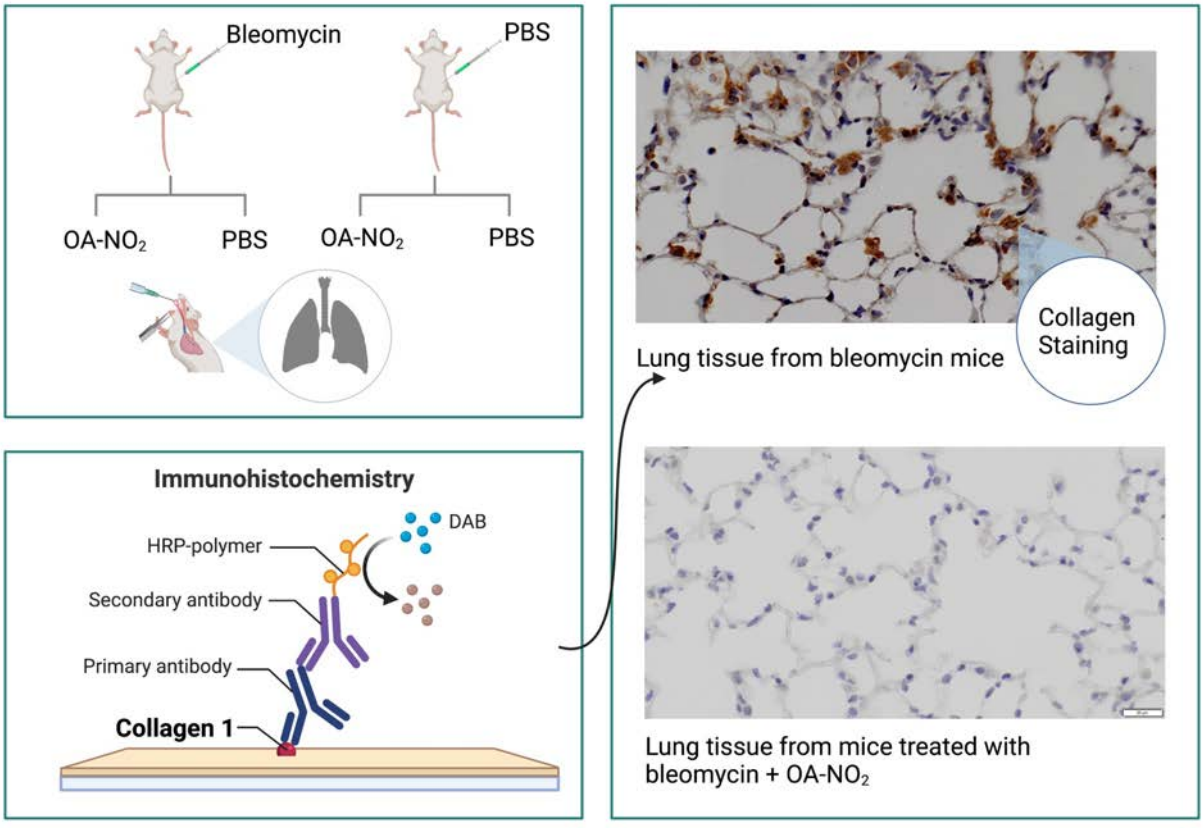
Each year in the United States, there are 190,600 cases of acute lung injury (ALI), associated with a mortality rate of over 74,000 deaths. Data shows acyl-coenzyme A acetyltransferase-1 (ACAT-1) inhibition improves pulmonary inflammation in an in vivo murine model of ALI. We hypothesize that ACAT-1 inhibition has anti-inflammatory effects beyond its intended use to reduce cholesterol esterification. The purpose of this study is to establish an in vitro bone marrow-derived macrophage (BMDM) model to investigate the effect of ACAT-1 inhibition in macrophage activation by inducing an inflammatory response through lipopolysaccharide (LPS), and selectively inhibiting ACAT-1 with K-604. This model will provide insight on target cell metabolism, reduce interference from whole-body effects, and minimize animal use. Monocytes were harvested from the bone marrow of 6-8 week old wild-type mice C57BL/6J (Jackson Laboratory) and stimulated with M-CSF on d0, 3, and 7 to induce macrophage differentiation. To examine if ACAT-1 inhibition limits macrophage activation, K-604 was co-administered with M-CSF. Then, the cells were treated with LPS on d7 and harvested after 24h. Nitrite, NOS2 expression, and iNOS protein were determined through nitrite colorimetric measurement, RT-qPCR, and western blot, respectively. Nitrite was measured as a proxy for nitric oxide (NO) production and was observed to decrease in LPS-stimulated cells chronically treated with K-604. NOS2 was also reduced in LPS and K-604 conjunctive treatment. Compared to LPS, iNOS was reduced with chronic K-604 as measured by iNOS protein. LPS-induced macrophage activation was suppressed and NO production was hindered due to lack of the iNOS protein. This aligns with the in vivo model, where K-604 reduced pulmonary inflammation in a rodent model of ALI. As LPS is known to increase cellular reliance on glycolysis, we will examine the effect of chronic K-604 on GLUT-1 transporter activity and PFKB1 protein expression. Supported by R25ES020721.



Nitrated Fatty Acid Inhibition of Bleomycin-Mediated Pulmonary Fibrosis

Perel Rose, Melissa L. Wilkinson, Andrew J. Gow
Rutgers, The State University of New Jersey

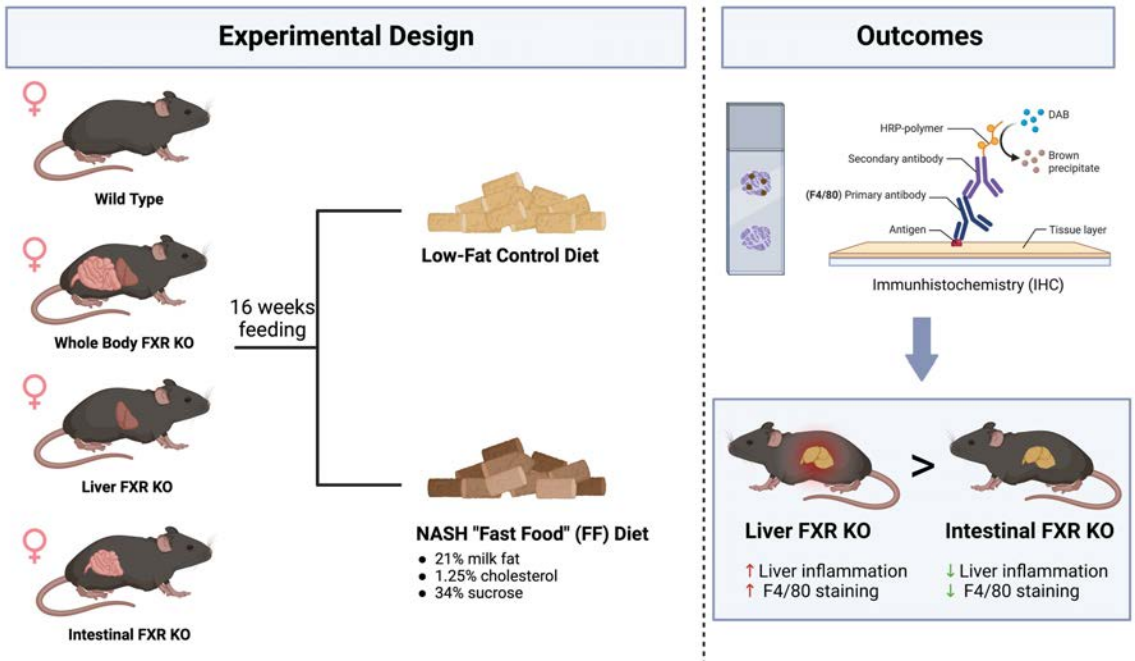
Interstitial lung disease (ILD) is highly prevalent in the United States, with limited treatment options leading to high morbidity and mortality. ILD is characterized by interstitial remodeling and fibrosis, which can be evaluated by collagen deposition. Nitrated fatty acids, such as nitro-oleic acid (OA-NO_2), are endogenously formed signaling mediators that have demonstrated anti-inflammatory and anti-fibrotic properties but have not been extensively studied in the lung. To assess their potential to improve fibrosis, an intraperitoneal bleomycin (IPB) model was employed. We hypothesize that OA-NO_2 will limit pulmonary fibrosis in a model of ILD based on its anti-inflammatory, pro-survival properties. C57BL6/J mice were injected with 0.1U IPB or PBS every 3d for 15d and were administered 50µg OA-NO_2 intratracheally on days 0, 4, 9, 16, 25, and 35. Mice were allowed to recover to 40d, after which lung tissue was collected for immunohistochemistry (IHC) and Mason's Trichrome staining to observe collagen deposition. In trichrome stained tissues, mice administered IPB had higher fibrosis scores than control mice (1±0.3 vs 4.5±1.3*score). This was mitigated by the administration of OA-NO_2 (2.5±2.3$^{\#\dagger}$). Increased collagen deposition in IPB mice compared to controls (5±2.7 vs 28±8.8*count), which was mitigated by OA-NO_2 administration (6±1.6†count), supported these findings. In summary, bleomycin-mediated increases in collagen deposition were mitigated by the administration of OA-NO_2, indicating its potential as an anti-fibrotic therapeutic in ILD. Supported by the ASPET SURF Intern Program and NIH R25ES020721.



Determining the Tissue-Specific Role of FXR in Inflammation Using Diet-Induced NASH Mouse Models

Sophie Gao, Zakiyah Henry, Bo Kong, Grace L. Guo
Rutgers, The State University of New Jersey

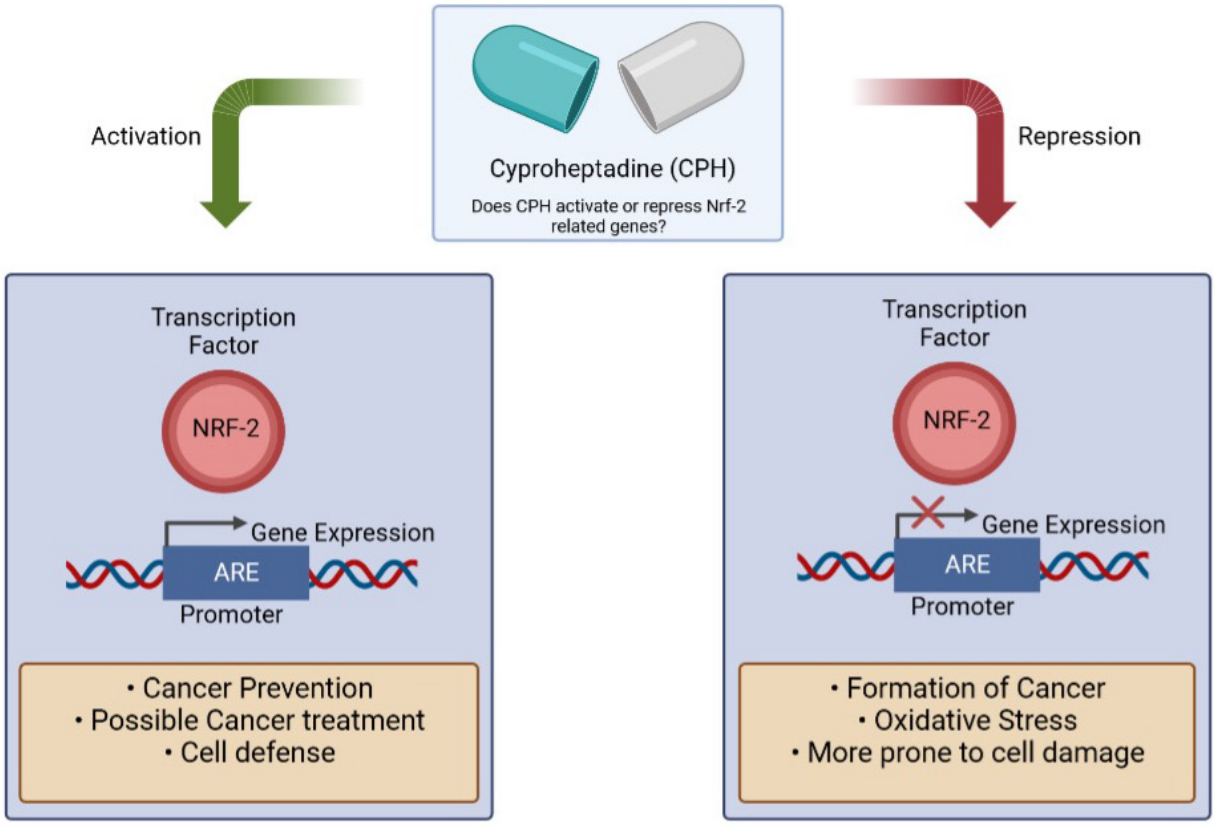
Non-alcoholic fatty liver disease (NAFLD) is a spectrum of diseases featured with over-accumulation of fat (steatosis) in the liver and it is estimated that over one third of the US population is affected by this disease. Non-alcoholic Steatohepatitis (NASH) is a more serious form of NAFLD, consisting of steatosis, inflammation, and fibrosis. Currently, there exists no FDA-approved treatment for NASH. The farnesoid X receptor (FXR) has been identified as a therapeutic target for NASH due to its ability to decrease steatosis, inflammation, and fibrosis. Synthetic ligands of FXR have been developed for therapeutic purposes but showed severe side effects as they are whole-body FXR activators; therefore, it is important to understand the tissue-specific functions of FXR in the development of NASH to design efficacious and safe therapeutics. To understand the underlying mechanisms of FXR tissue-specificity, 6-8 week old female mice in 4 genotypes: wild-type (WT, C57BL/6J, Fxr+/+), liver FXR knockout (KO) ((Fxrfloxed/floxed, Albumin Cre (+), FXR LKO), intestinal FXR KO (Fxrfloxed/floxed, Villin Cre (+), FXR IKO), and whole-body FXR KO (WB FXR KO, Fxr-/-), were fed either a low-fat control diet (CTL) or a NASH “Fast Food” (FF) diet (Western diet with 21% milk fat, 1.25% cholesterol, and 34% sucrose) for 16 weeks. Liver samples were collected for histology and sections were stained with F4/80, a macrophage marker to indirectly measure inflammation, to distinguish differences in macrophage abundance among groups. The FXR LKO mice fed the FF diet displayed significantly increased F4/80 staining compared to the FXR IKO group. The FXR LKO on the CTL diet showed a trending increase compared to the FXR IKO. Both the FXR KO and FXR IKO groups displayed positive staining for F4/80 at levels comparable to the WT regardless of the diet. These data suggest that FXR LKO is more critical to suppressing hepatic inflammation compared to FXR IKO. As a result, targeting hepatic FXR opposed to intestinal FXR may be more beneficial to treat liver inflammation present during NASH. Funding: ASPET SURF Program, NIH R01GM135258-01A1S1, GM135258, ES029258, DK122725 and the VA BX002741.



Investigating Cyproheptadine as an NRF2 Activator in Human Liver Cancer Cells

Mohammed Khedr, Pochung Jordan Chou, Ah-nNg Tony Kong
Rutgers, The State University of New Jersey

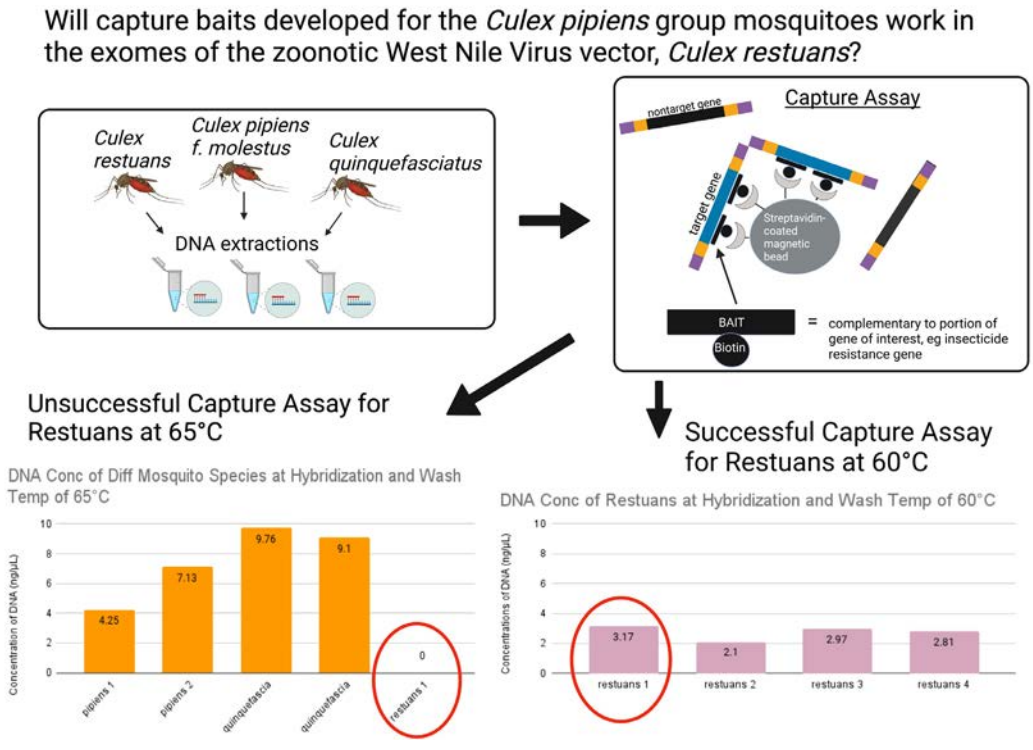
The buildup of free radicals due to UV radiation and the body's metabolism can cause damage and mutations in DNA, leading to the formation of tumors and cancers. The NRF2-ARE pathway has been studied and is identified as a pathway against oxidative stress. Cyproheptadine (CPH), an FDA-approved allergy medication, has reported its effects on histamine and serotonin. We sought to investigate the antioxidant properties of Cyproheptadine and its mechanism by studying the NRF2-ARE pathway in HepG2 cells. The cytotoxicity of CPH was first tested by treating the cells with different concentrations (0- 30 uM) of CPH for 24h using the MTS assay. The influence of CPH on the NRF2-ARE pathway was investigated by ARE-Luciferase assay and qPCR assay. The cytotoxic result indicated CPH exhibited above 70% cell viability at 20 uM. At 15 uM of CPH, it was observed to have an activity fold change 3 times higher than the control group ($p < 0.01$) in the ARE-Luciferase assay, suggesting CPH is a potential Nrf2 activator. Therefore, we next examined the expression of Nrf2-related genes (HO-1, NQO1) using qPCR. These genes (NRF2, HO-1, NQO1) were more expressed with higher concentrations of CPH (15 - 20 uM) than the control. In this study, CPH plays an activator of the NRF2-ARE pathway, indicating its potential role against cancer. Supported by R25ES020721.



Test of an Exomic Capture Assay To Identify and Sequence Insecticide Resistance Genes in Non-Model Mosquitoes

Kaitlyn Fang, Nicole Wagner, Dina M. Fonseca
Cornell University and Rutgers, The State University of New Jersey

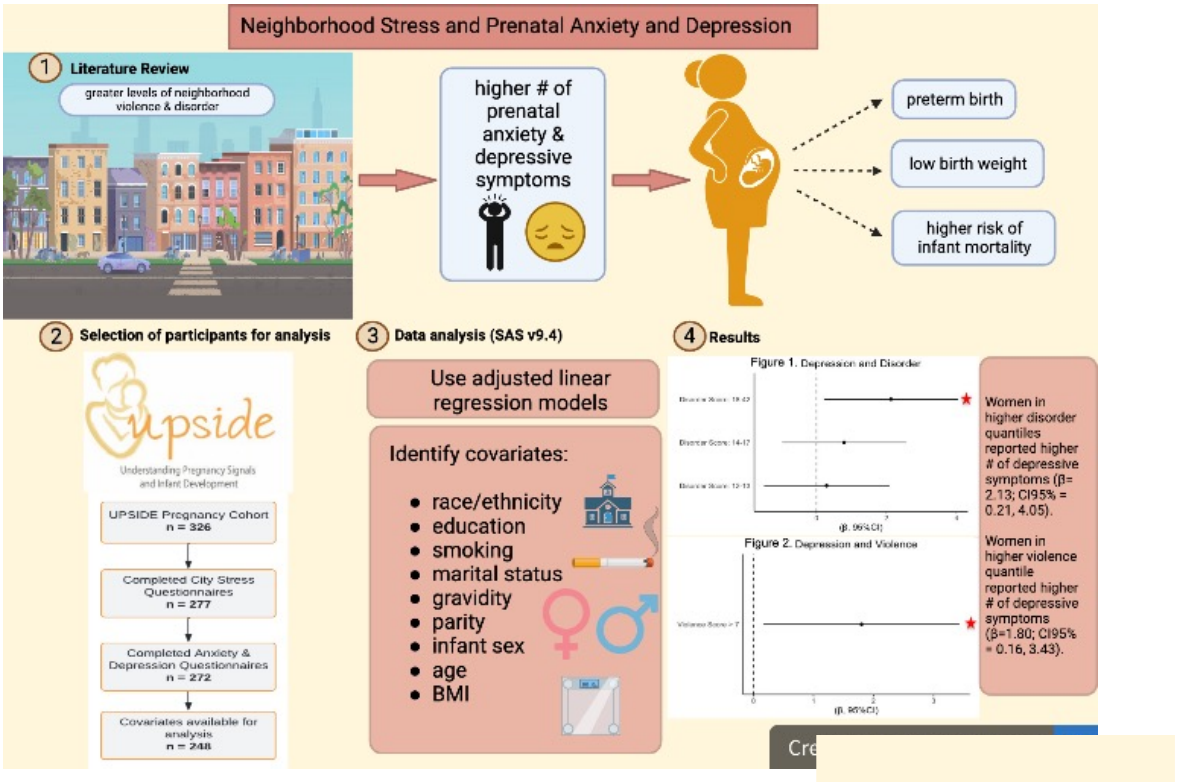
While yellow fever, dengue, and Zika are transmitted between humans by human biting mosquitoes, West Nile virus, eastern equine encephalitis and many other deadly human pathogens are zoonosis. The amplifying hosts of the viruses are birds and critical transmission among birds and spillovers to humans occurs by mosquitoes, such as *Culex restuans,* for which genomic information is very limited. We tested the use of a capture assay developed for *Culex pipiens* group mosquitoes, that among others targets all ~350 genes known to be associated with insecticide resistance in mosquitoes. We developed a side-by-side comparison by testing the bait capture in specimens from the *Cx. pipiens* group and *Cx. restuans.* We developed NextGen genomic libraries from existing DNA samples. After the bait hybridization with a temperature of 65℃ the average DNA concentration for *Cx. quinquefasciatus* was 6.98 ng/µL, for *Cx. pipiens f. molestus* was 5.48 ng/µL while the *Cx. restuans* was too low for readings to be measured even with a highly sensitive Qubit Fluorometer. To address this, we lowered the hybridization temperature to 60℃, therefore lowering the stringency and allowing slightly variable sequences to still anneal to the baits. The resulting DNA concentrations for the *Cx. restuans* were on average 2.76 ng/µL. In conclusion, the capture assay was successful although subsequent NextGen sequencing will determine the extent of the success. These results suggest that the gene-based capture assay is a cost-effective strategy to obtain information on insecticide resistance in mosquitoes, and ultimately help develop better strategies to limit its spread. Supported by R25ES020721.



Neighborhood Stress and Prenatal Anxiety and Depression

Michaela Greenlee, Megan Hansel, Emily S. Barrett and Zorimar Rivera-Núñez
Rutgers, The State University of New Jersey

Public health research has been focusing increasingly on the environmental and social factors that may influence adverse maternal health outcomes, rather than only the individual-level factors (e.g., personal behaviors and genetic or biological make-up). Neighborhood characteristics have been associated with residents' quality of mental health. Mental wellbeing is critical during pregnancy, as mental health disorders relate to complications, including preterm birth and infant mortality. We hypothesized that pregnant women living in neighborhoods experiencing greater social disorder and violent events will report higher levels of anxiety and depression. 326 pregnant women were recruited through the Understanding Pregnancy Signals and Infant Development cohort in Rochester, New York. Neighborhood stress was measured using the City Stress Inventory Questionnaire, while anxiety and depression were measured using the Penn State Worry Questionnaire and the Edinburgh Postnatal Depression Scale, respectively. Using Statistical Analysis System (SAS) v9.4 software, we utilized linear regression models adjusted for maternal age, race, ethnicity, marital status, education, BMI, smoking, parity, gravidity and fetal sex. Participants in the higher neighborhood disorder quantiles reported a higher number of depressive symptoms (β = 2.13; CI95% = 0.21, 4.05) compared to those in the lowest disorder quantile. Additionally, participants reporting neighborhood violence quantile scores reported a higher number of depressive symptoms (β = 1.80; CI95% = 0.16, 3.43) compared to women reporting no neighborhood violence. There was no statistically significant association between neighborhood disorder or violence and anxiety. Our results suggest that neighborhood stressors can adversely impact depressive symptoms during pregnancy. Public health interventions targeted towards alleviating neighborhood stressors may improve prenatal mental health which, in turn, may produce more favorable birth outcomes. Supported by R25ES020721.

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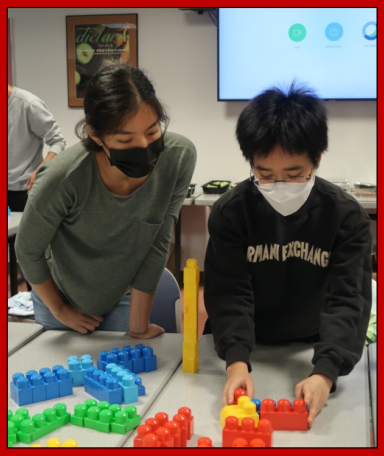
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